Paid Circulation, 32,903

Annual Meeting
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The New England Journal of Medicine

FORMERLY THE BOSTON MEDICAL AND SURGICAL JOURNAL — *Established 1828*

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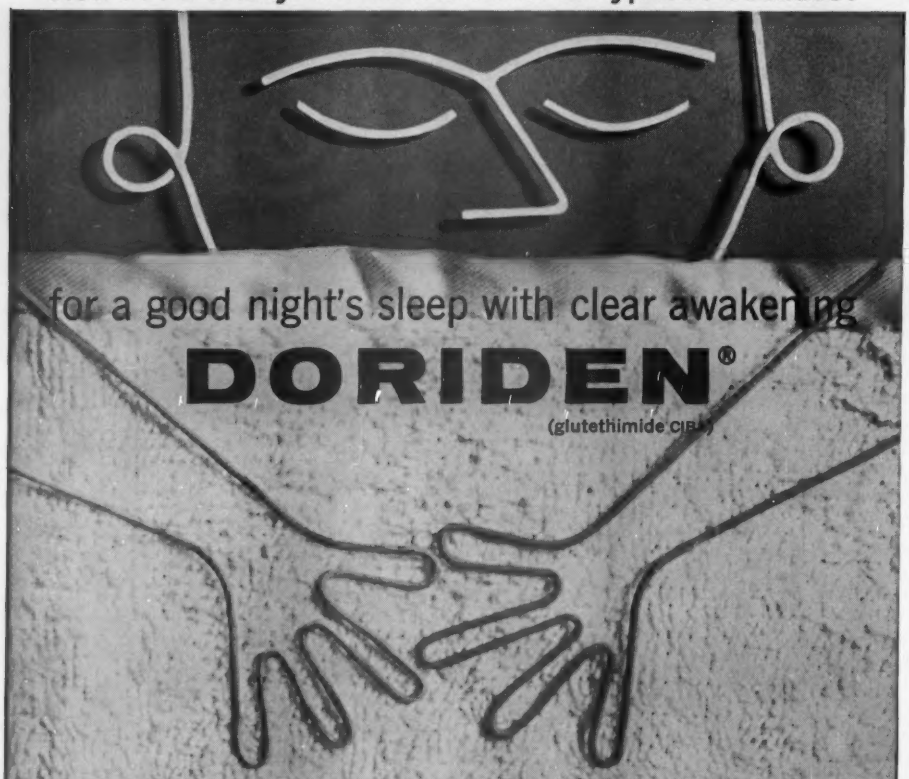

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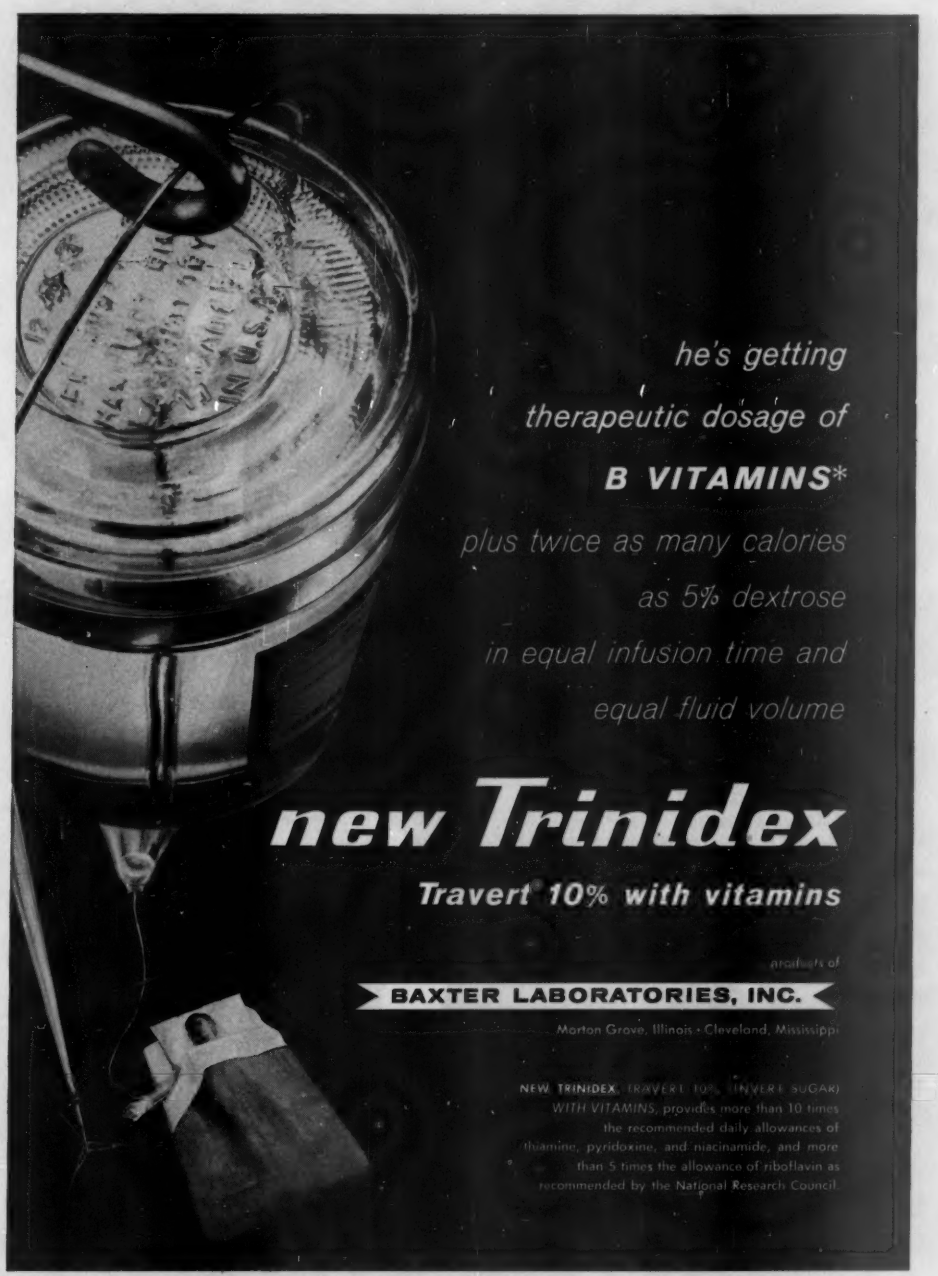
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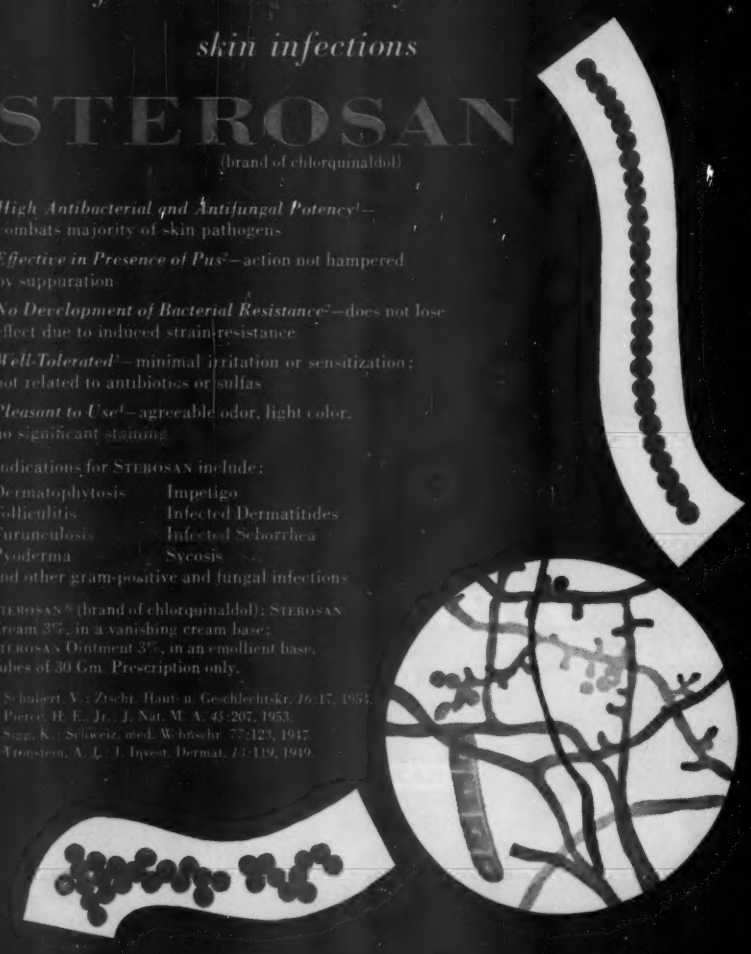

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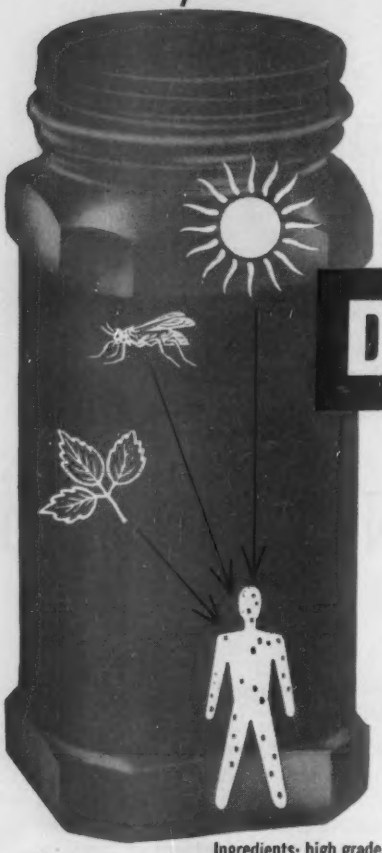

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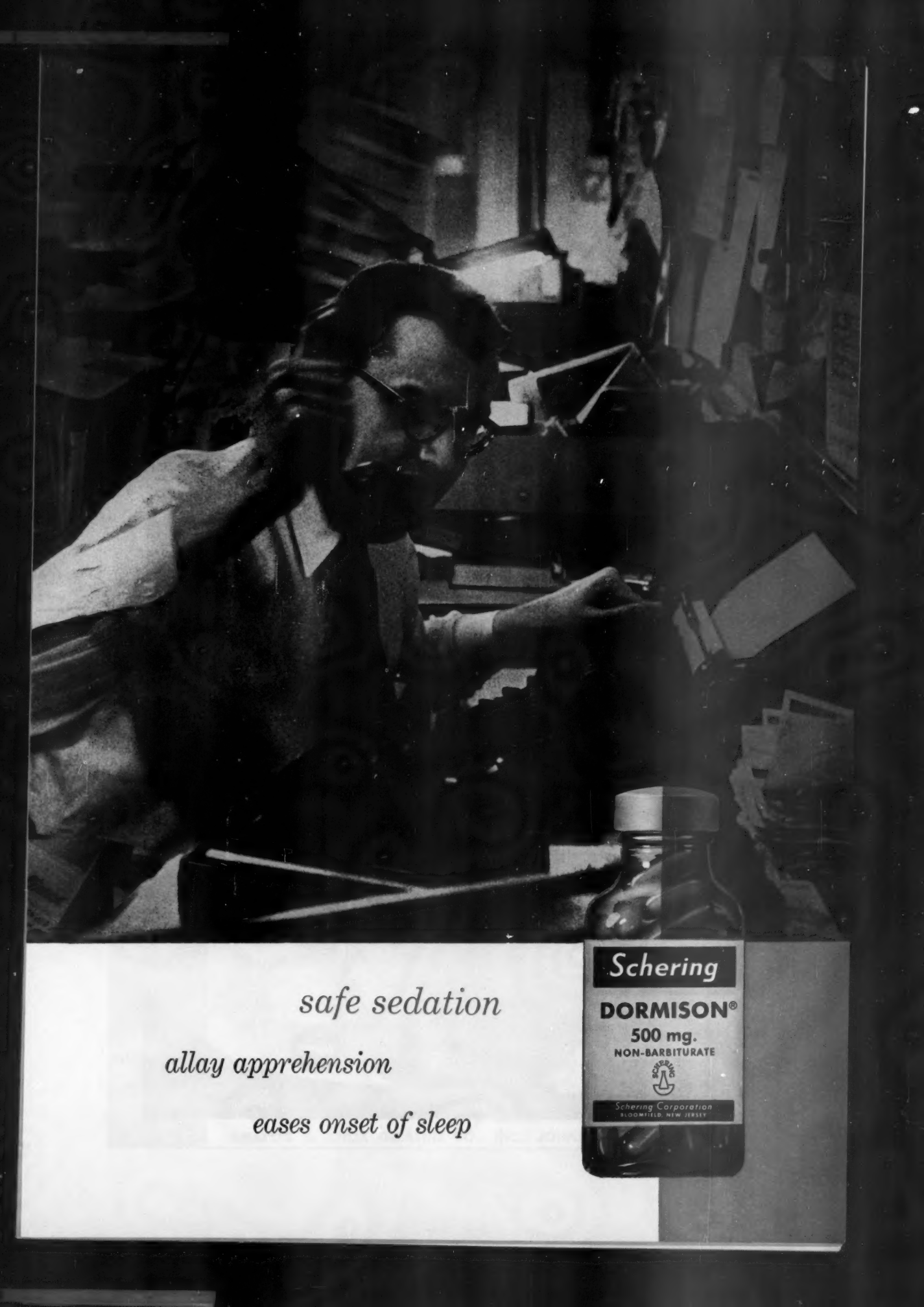

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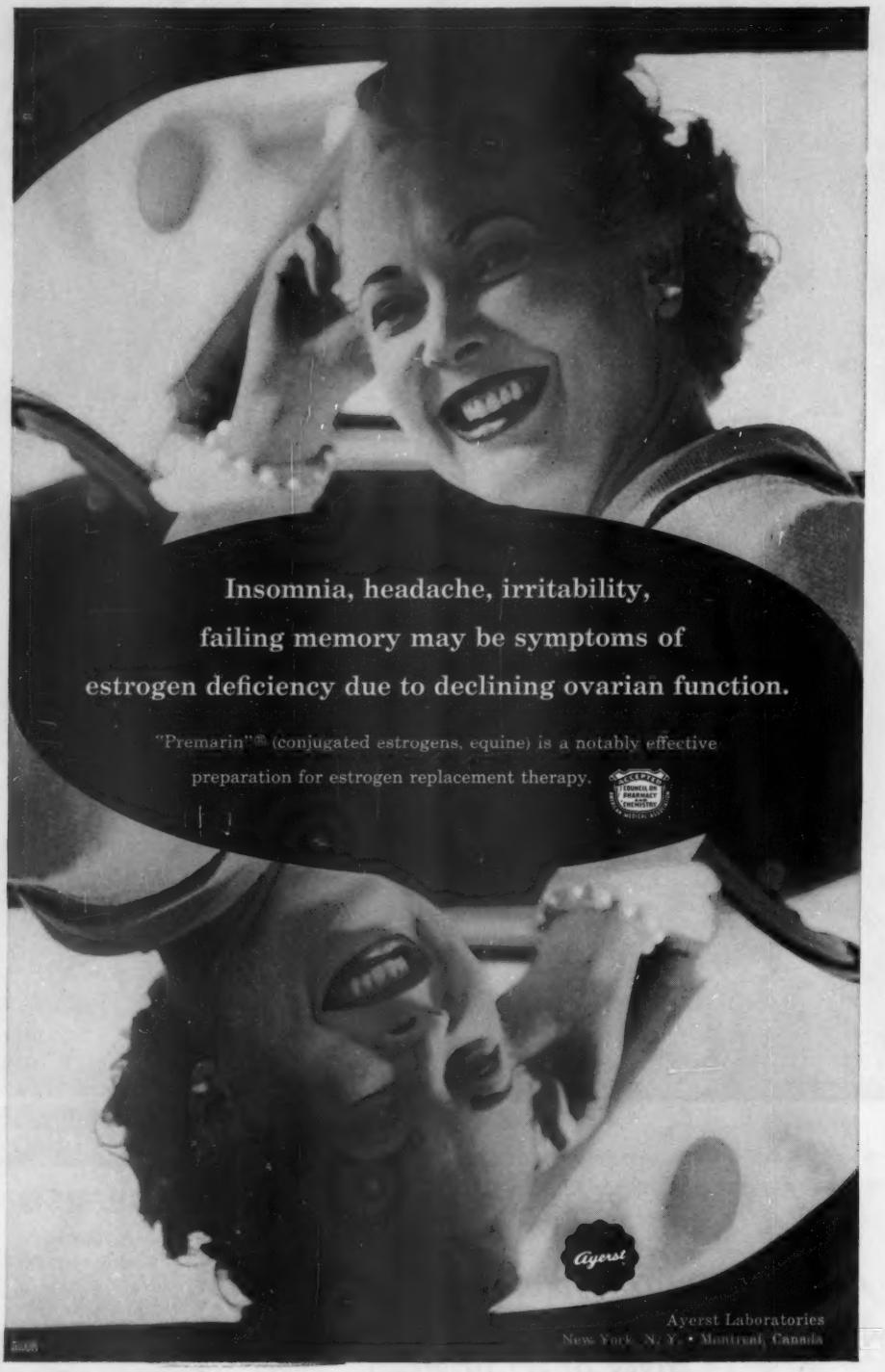
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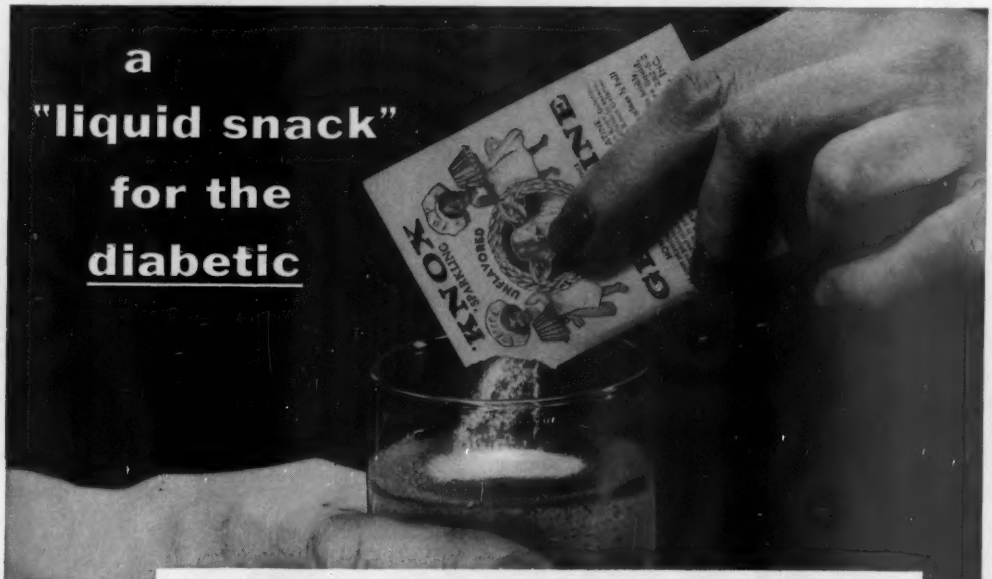

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Volume 252 APRIL 14, 1955 Number 15

MODERN CONSIDERATIONS OF MAJOR HAND INFECTIONS*

J. Edward Flynn, M.D.†

BOSTON

LYMPHANGITIS, deep-fascial-space abscess and acute suppurative tenosynovitis are the major infections of the hand. Usually, one of these conditions exists in a single patient. However, on rare occasions, more than one may occur simultaneously. A knowledge of the anatomy involved is basic for a proper understanding of the clinical aspects and treatment of each of these entities.

Lymphangitis

Lymphangitis may be defined as an acute inflammatory process of the lymphatic vessels. There are two types of lymphangitis of the upper extremity, superficial and deep. The former involves the superficial vessels that arise in the skin. The collecting trunks of superficial lymphatics run in the subcuticular tissue.

The superficial lymphatics of the fingers consist of volar and dorsal networks that converge into trunks at the sides of the fingers. The digital trunks reach the bases of the fingers in the interdigital spaces and traverse the dorsal aspect of the hand to the wrist. The network of superficial lymphatics of the palm drain into trunklets that divide into external, internal, inferior, superior and central vessels. In the wrist there are two groups, volar and dorsal.

The superficial lymphatics diminish in number as they go up the arm (Fig. 1). Sappey[1] states that they number about 30 in the forearm and from 15 to 18 in the middle of the arm. In the forearm, the volar vessels divide into three groups — external, internal and median. In this part the volar lymphatics are more numerous than the dorsal lymphatics. In the arm, the trunks unite into a single bundle on the external surface. The majority of collecting vessels terminate in the axilla in the humeral chain of axillary lymph nodes. Two or three of the most internal end in the epitrochlear lymph node, whose efferent vessels perforate the deep fascia in the middle of the arm and end in the deep vessels. When this node is absent, the internal collecting vessels may perforate the fascia at the same point to reach the deep absorbing vessels. The most external trunk separates itself from the other collecting vessels in the region of the humeral insertion of the deltoid and ascends in the deltopectoral groove, where it may traverse one or several nodes. This trunk usually passes into a subclavian node, placed at the spot where the cephalic joins the axillary vein. Mascagni[2] says that it may pass above the clavicle and empty into the supraclavicular node. Grossman states that this arrangement occurs in 38 per cent of cases.

The deep lymphatics follow the brachial artery and its chief branches, usually with two lymphatic trunks for each artery. The deep lymphatics of the upper extremity may be divided into radial, ulnar, anterior interosseous, posterior interosseous and humeral. The radial trunks drain lymph from the part supplied by the deep volar arch and the superficial palmar branch of the radial artery. They ascend the forearm as far as the bend of the elbow. The ulnar trunks drain lymph from the part supplied by the superficial volar arch and the deep and dorsal branches of the ulnar artery. The anterior interosseous and posterior interosseous lymphatics follow the arteries of the same names. The humeral trunks are two or three in number. They run by the side of the brachial artery and terminate in the humeral chain of axillary lymph nodes (Fig. 2).

Symptomatology

Kanavel[3] stressed the importance of differentiating lymphangitis from other major infections of the hand and reiterated the need to distinguish superficial from deep lymphangitis. With superficial lymphangitis, there is usually a history of an abrasion or superficial wound of the hand. General signs of infection — fever, leukocytosis, nausea, vomiting and tachycardia may be present. Red streaks extend up the forearm and arm. Superficial lymphangitis usually lacks the rapid and great swelling of the entire hand and forearm. With deep lymphangitis, there is a history of a deep infection, such as osteomyelitis. The general signs of infection are more pronounced than those found with superficial lymphangitis. Red streaks may

*Presented at the fortieth annual clinical congress of the American College of Surgeons, postgraduate course, Atlantic City, New Jersey, November 16, 1954.

†Assistant clinical professor of surgery, Tufts College Medical School; assistant visiting surgeon, First Surgical Service, Boston City Hospital; attending surgeon, Boston Veterans Administration Hospital; visiting surgeon, St. Elizabeth's Hospital.

or may not be seen. The outstanding differential point is that, with deep lymphangitis, there is usually a rapid and striking increase in swelling of the entire hand and forearm. With lymphangitis there is voluntary movement of fingers without pain, absence of pain on hyperextension of fingers and thumb, absence

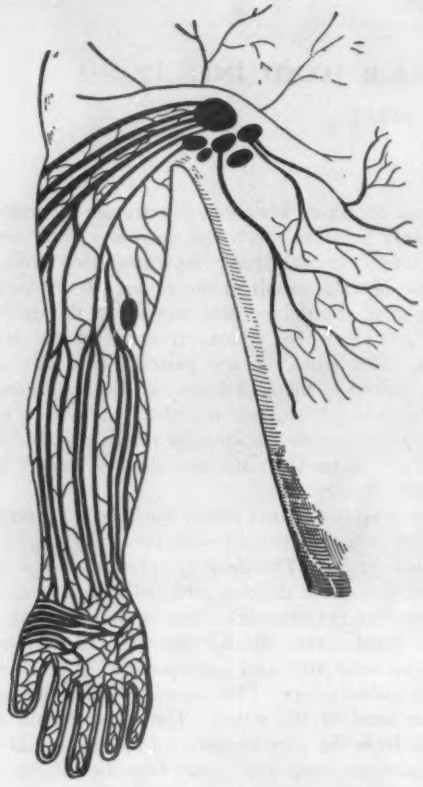

FIGURE 1. *Schematic Drawing of the Superficial Lymphatics of the Upper Extremity.*

of tenderness over tendon sheaths, absence of bulging of the palm and absence of tenderness over the midpalmar and thenar spaces.

Prevalence

Lymphangitis is estimated to be between 15 and 25 per cent as frequent as it was before antibiotics.

Treatment

Local measures to wall off and overcome the infection, together with procedures designed to support the system, increase its resisting power and eliminate toxins, and antibiotics are necessary. In cases of lymphangitis, until localization is present, warm saline dressings should be used, and hospitalization should be insisted upon, with local and generalized rest, together with cathartics, adequate electrolyte and fluid intake, sedatives and usually penicillin.

Warm saline dressings are used locally to produce hyperemia; their value in combination with antibiotics has been challenged. The arm is placed on a sterile towel, and sterile dressings, wet with warm saline solution, are applied. The dressings are covered with rubber sheeting, which is enveloped in towels. Two perforated rubber tubes are inserted in the gauze pack, through which warm saline solution may be introduced every two hours. The heat is maintained by the use of hot-water bottles. In severe cases the dressings are applied to cover the entire arm and shoulder. The part covered is always larger than the area involved in the infection. This dressing usually provides adequate splinting.

Hospitalization, with local and systemic rest, should be insisted upon, especially in severe infections. Immobilization is necessary because every movement of muscles of fingers, hand, forearm and arm favors lymphatic circulation and dissemination of infection.

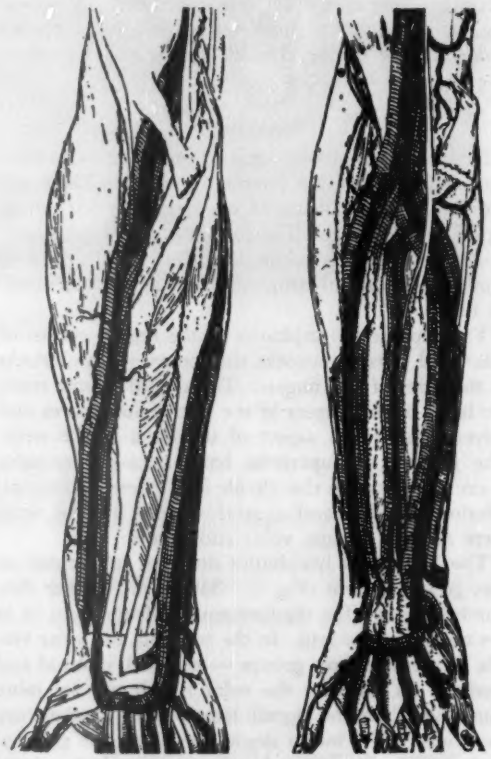

FIGURE 2. *Schematic Drawing of the Deep Lymphatics of the Upper Extremity.*

The hand and arm should be elevated on pillows to allow proper lymphatic drainage.[4]

Seriously ill patients should be given much fluid and small amounts of easily digested food. Large amounts of fluids are of great value in diluting and eliminating toxins. Penicillin is a specific antibody for most organisms that cause lymphangitis. Usually, 100,000

units is given every four hours until there is no sign of infection and the temperature has been normal for twenty-four hours. When a wound is present a culture is taken, and sensitivity tests are performed.

The basic principles in treating infection must be exercised, especially with more frequent reports of resistance of pyogenic organisms to antibiotics.[5]

Complications

The complications of lymphangitis have been greatly decreased since the advent of antibiotics but still occur, usually some time after antibiotic therapy has been discontinued. The possibility of their occurrence should be kept in mind.

An understanding of the anatomy involved explains certain complications. The superficial lymphatics run in the subcutaneous tissue and may cause extensive subcutaneous destruction of connective tissue, with the formation of slough and thin streptococcal pus as a most serious complication that is treated by incision and drainage, usually on the dorsum. The superficial lymphatics, especially, empty into epitrochlear, axillary, deltopectoral, supraclavicular and other lymph nodes, abscesses of which are treated by incision and drainage. Subpectoral abscesses arise from infected nodes. Rarely, a large quantity of pus fills the axilla and extends under the pectoral and subscapular muscles, and must be drained. Subclavicular and shoulder abscesses are very rare and develop along the course of the lymphatics lying in the pectorodeltoid groove. Such infections most commonly have their origin in the middle finger. The deep lymphatics are close to tendon sheaths and may cause suppurative tenosynovitis. The humeral chain of axillary nodes eventually empty into the thoracic duct and general circulation, and may be the cause of septicemia or pyemia.

Deep-Fascial-Space Abscess

A knowledge of the anatomy of the deep fascial spaces is necessary for the understanding of the signs and treatment of abscesses of the palm. Since Kanavel[2] described these deep surgically important spaces as the midpalmar and thenar, there has been some controversy about their anatomy.[6,7] In 100 cases in which dissection was performed with special consideration of the fascial distributions[8] there was a definite septum of fascia coming from the undersurface of the flexor tendons of the middle finger, which was attached to the entire length of the middle metacarpal bone (Fig. 3). This septum divides the palm into two fascial compartments, the midpalmar and thenar spaces. It is convenient to remember that the deep fascial spaces are deep to the flexor tendons. The midpalmar space extends from the middle metacarpal bone ulnarward to the radial side of the fifth metacarpal bone. Anteriorly, this space is bounded by the flexor tendons of the middle, ring and little fingers, the third and fourth lumbrical muscles and the thin fascia that connects these tendons and muscles.

The posterior boundary or floor is formed by the fascia covering the second and third volar interosseous muscles, and the third, fourth and fifth metacarpal bones. In the distal third of the floor, small compartments are formed, since septums coming from the undersurface of the palmar aponeurosis are attached

Figure 3. *Middle Palmar Septum Dividing the Palm into the Midpalmar and Thenar Spaces.*

to the fascia of the volar interosseous muscles. These small compartments communicate with the midpalmar space. The medial boundary is the fascia on the radial side of the hypothenar muscles. The lateral boundary is the midpalmar septum, which extends from the undersurface of the flexor digitorum profundus tendon of the middle finger to the middle metacarpal bone (Fig. 4). Distally, the midpalmar space extends about 2 cm. proximally to the webs. The distal boundary is composed mainly of fascial septums extending from the palmar aponeurosis to the floor of the space and to some transverse fasciculi. The proximal boundary is a thin fascial septum usually found at the level of the proximal end of the transverse carpal ligament.

The thenar space is bounded posteriorly by the adductor pollicis muscle. Medially, the boundary is the midpalmar septum, a thin fascia extending from beneath the flexor digitorum profundus tendon of the middle finger to the third metacarpal bone (Fig. 5). Proximally, in all cases, this fascia, which is a part of the adductor fascia, forms the boundary. The proxi-

mal boundary is found at about the level of the distal end of the transverse carpal ligament. The anterior boundary or roof is the thin layer of fascia formed as the midpalmar septum splits and courses laterally. In its lateral course this fascia ensheaths the flexor tendons of the index finger to form part of the an-

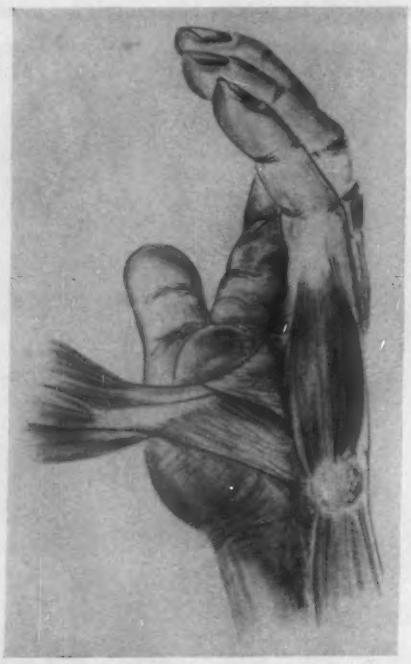

FIGURE 4. *Middle Palmar Septum Forming the Lateral Boundary of the Midpalmar Space.*

terior boundary. The lateral boundary of the thenar space is formed by the thin fascia as it extends over the lateral edge of the adductor pollicis muscle and is attached to the dorsal aspect of this muscle. This distribution of fascia over the anterior, lateral and dorsal aspects of the adductor pollicis muscle clearly indicates why abscesses of the thenar space may extend to the posterior aspect of the muscle. The fact remains, however, that abscesses of the space tend to remain anterior to the adductor pollicis muscle.

The midpalmar septum, which separates the midpalmar space from the thenar space, is a thin structure but is apparently adequate to keep an infection confined to one space. In a review of 100 cases of deep-fascial-space infection, both the thenar and midpalmar space were involved in only 2 cases, and in each case, extensive local necrosis and osteomyelitis were found.[9]

Clinical Observations

Prevalence. Infections of the deep fascial space have been much less frequent since the advent of antibiotics. Previously, of 100 cases studied at the Boston City Hospital over a seven-year period,[8] the thenar space was involved in 70, and the midpalmar space in 30 cases. In the past five years at the Boston City Hospital there have been 14 cases, the thenar space being involved in 10 and the midpalmar space in 4.

Since the advent of antibiotics, deep fascial space abscesses have occurred about a fifth as frequently as before antibiotics, at the Boston City Hospital. Diabetes has complicated most of the cases encountered in the past five years.

Etiology. In this series of 100 cases the commonest cause of thenar-space abscess was puncture wounds. Suppurative tenosynovitis was next in frequency; it is interesting that thenar-space abscess developed in 2 cases of suppurative tenosynovitis of the middle finger. Other causes were septic abrasions, septic blebs, cellulitis, subcuticular abscess, burns, osteomyelitis, septic laceration, septic callus and lumbrical-space abscess of the index finger.

FIGURE 5. *Middle Palmar Septum Forming the Medial Boundary of the Thenar Space.*

The commonest cause of midpalmar-space abscess was lumbrical-space abscess of the ring finger. Puncture wounds were second in frequency. Other causes were septic abrasions, suppurative tenosynovitis, septic blebs, cellulitis, osteomyelitis and septic lacerations. It is of interest that midpalmar-space abscess developed in 2 cases of tenosynovitis of the middle finger.[8]

Differential Diagnosis. Tenderness over the palmar aspect of the space involved is the most important sign. With thenar-space abscess, swelling rapidly in-

creases the size of the thenar area. With midpalmar-space abscess, the swelling obliterates the concavity of the palm. There is usually greater swelling over the dorsum of the hand with both infections. Position of the fingers is of some value. The index finger is usually flexed when the thenar space is involved. The middle and ring fingers are flexed with midpalmar-space abscess.

Treatment. Since the advent of antibiotics, some have advocated the aspiration of pus and instillation of penicillin into the involved space. Others have advised excision, with suture technic.[10] These procedures appear illogical for serious infections. The best treatment is incision and drainage. When the diagnosis is made, one should not delay with antibiotics as the sole therapeutic procedure. A pneumatic tourniquet is used for hemostasis.

The thenar space is best drained by an incision over the dorsum of the thumb-index web, at the middle of a line drawn between the distal ends of the metacarpal bones of the thumb and index fingers, with the thumb abducted. This incision is carried through the subaponeurotic fascia that forms the lateral boundary of the thenar space. Pus may be found dorsal to the adductor pollicis muscle. A hemostat is then carried over the superior edge and anterior surface of the adductor pollicis muscle, and pus is drained from the space. Slough is removed. The space is irrigated with physiologic saline solution; 50,000 units of penicillin in 5 cc. of saline solution is injected into the space. A rubber tissue drain may be used for twenty-four to forty-eight hours, when there is much edema, to keep wound edges separated.

The midpalmar space is drained by a transverse incision through or at the place of maximum tenderness on a line parallel with the distal transverse crease. This incision is carried transversely through skin, superficial fascia and palmar aponeurosis. The digital vessels and nerves are retracted with the flexor tendons. Usually, a point between the flexor tendons of the middle and ring fingers is entered. This latter incision is placed longitudinally through the thin subaponeurotic fascia between the flexor tendons, and enters the midpalmar space. Slough is removed, and the space is irrigated with saline solution; 100,000 units of penicillin in 5 cc. of saline solution may be inserted into the space, and a drain may be used for forty-eight hours.

A culture of the pus is taken, and sensitivity tests are performed. Postoperatively, the hand is immobilized with an aluminum splint in a position of function until the infection subsides. Hot fomentations are used, and 100,000 units of penicillin is given intravenously immediately after operation; 100,000 additional units is given intramuscularly every three hours until infection subsides, when active motions are begun. The fomentations are used until cellulitis subsides and never to a point of waterlogging.

Acute Suppurative Tenosynovitis

Suppurative inflammation of the flexor-tendon sheaths of the hand presents a controversial problem. A knowledge of the anatomy of the sheaths is basic for the proper treatment of suppurative tenosynovitis. The synovial sheaths of the flexor tendons for the index, middle and ring fingers extend from about the distal transverse crease of the palm to the bases of the distal phalanges. For clinical purposes it must be considered that in nearly all cases the sheath of the flexor pollicis longus is continuous with the radial bursa. Poirier and Cuneo[11] report that in 19 of 20 cases the sheath of the flexor pollicis longus was continuous with the radial bursa. The sheath of the flexor tendons of the little finger is continuous with the ulnar bursa in about half of all cases according to these authors, but others believe that the connection occurs more frequently. Kanavel[3] states that the communication between the radial and ulnar bursa is frequent, occurring in about half his cases.

Kanavel[3] described an intermediary posterior palmar sheath connecting the radial and ulnar bursas in 80 per cent of dissections, and an anterior intermediary palmar sheath in 50 per cent.

Prevalence

Over a five-year period, and before the introduction of antibiotics, from 1938 through 1942, 100 cases of acute suppurative tenosynovitis were encountered at the Boston City Hospital. With the advent of antibiotics, 50 cases were seen over a six-year period (1943 to 1948), or about 42 per cent of the frequency before antibiotics. For the past five years (1949 to 1953) the average has been about 5 cases a year. These series indicate that acute suppurative tenosynovitis now is about a fourth as common as before antibiotics.

Etiology

The origin of the infection is either direct inoculation of the tendon sheath or an indirect one in which the infection spreads from a neighboring pathologic process. In the series at the Boston City Hospital 59 per cent were of direct, and 41 per cent of indirect origin. Puncture wounds are the most common type of injury causing septic tenosynovitis. In infections of direct origin, puncture wounds occurred in 37 per cent, lacerations in 18 per cent, and compound dislocation and gunshot wounds in 2 per cent each. In infections of indirect origin, puncture wounds occurred in 5 per cent, lacerations in 12 per cent, abrasions in 8 per cent, human bite and felon in 6 per cent each, contusions and burns in 2 per cent, and blebs and callus in 1 per cent each.[12]

Classification

The cases were classified on the basis of functional results[13] as follows:

Group 1. Results were considered optimum in cases with normal or almost normal function of tendons and those with complete or almost complete motion of all finger joints. There was sometimes slight limitation of extreme flexion. Function of fingers was practically as good as before infection. Active flexion in each interphalangeal joint was about 90°. On flexion, the tip of the finger touched or almost touched the palm.

Group 2. Cases with fair results included partial function of tendons, the limitation usually being caused by adhesions, and active but limited motion in the proximal and distal interphalangeal joints, or both. Motion in the metacarpophalangeal joint might be normal or slightly limited; a fist could not be made actively. Active flexion in each interphalangeal joint was at least 45° or the equivalent. When the patient was helped to make a fist, the tip of the finger reached to within 2 cm. of touching the palm.

Group 3. Poor results included sloughed tendons with loss of flexion of the middle or distal phalanx or both, and ankylosed proximal or distal interphalangeal joint, causing a stiff finger (motions in the metacarpophalangeal joint might not be present) as well as amputations and deaths. Active flexion of each interphalangeal joint was less than 45° or the equivalent. When the patient tried to make a fist the tip of the finger did not reach to within 2 cm. of touching the palm.

With antibiotics as an adjunct to surgery, the number of optimum results has been more than doubled, and the number of poor results is about a third of what it was before the use of antibiotics. Table 1 shows the comparative end results in both series.

TABLE 1. *Comparative End Results.*

TREATMENT	PERIOD	NO. OF CASES	GOOD RESULT	FAIR RESULT	POOR RESULT
			%	%	%
Operation without antibiotics	1930 - 1942	100	33	20	47
Operation in addition to antibiotics	1943 - 1953	75	68	16	16

TABLE 2. *Bacteriology Since the Advent of Antibiotics.*

ORGANISM	CASES IN GROUP 1	CASES IN GROUP 2	CASES IN GROUP 3
Streptococcus haemolyticus	14	3	2
Str. viridans	3	1	0
Staphylococcus aureus	10	2	1
Staph. albus	3	0	0
Str. haemolyticus & Staph. albus	4	2	3
Str. haemolyticus, Staph. aureus & diphtheroids	0	0	1
Str. haemolyticus, Proteus vulgaris & Borrelia vincentii	0	0	1

Bacteriology

Table 2 summarizes the bacteriology since the advent of antibiotics.

Complications

The frequency and severity of all complications have decreased since the use of antibiotics (Table 3).

Treatment

Since the advent of antibiotics more investigations of acute suppurative tenosynovitis than of the other major hand infections have been reported.

Five types of treatment have been suggested for acute suppurative tenosynovitis since the use of antibiotics: antibiotic therapy alone in the early stages; intra-arterial injection of penicillin as an adjunct to surgery; removal of pus, with irrigation, application or instillation of an antibiotic locally; excision, with suture technic (excision of slough and necrotic tissue and suture after incision); and adequate incision and drainage with antibiotic therapy parenterally.

TABLE 3. *Comparative Complications.*

COMPLICATION	FREQUENCY IN OPERATIONS WITHOUT ANTIBIOTICS	FREQUENCY IN OPERATIONS WITH ANTIBIOTICS
	%	%
Mortality	2	0
Amputations	18	8
Tendon slough	41	6
Osteomyelitis	31	12
Thenar-space abscess	18	2
Midpalmar-space abscess	12	2
Septic arthritis	9	2
Radial bursitis:		
In palm	10	2
At wrist	8	0
Ulnar bursitis:		
In palm	6	0
At wrist	3	0
Abscess of intermuscular space of forearm	3	0

Some have advised parenteral administration of penicillin as the sole form of treatment for twenty-four to forty-eight hours after onset[14] or early in the disease.[15] I believe that there should be no delay in surgery because I have seen cases of sloughed tendons within forty-eight hours of onset.[13]

Intra-arterial injection of pencillin has been recommended for the treatment of acute suppurative tenosynovitis.[16] The reason seems to be that there is an excess of edema in the infected region and that intra-arterial administration may give a locally increased concentration of penicillin in the infected site. The possible dangers with this route outweigh the possible good, especially the danger of arterial spasm in a region with a damaged circulation.

Various types of local antibiotic therapy have been

described; there is probably no place for these procedures. Adequate incision and drainage, as soon as the diagnosis is made, followed by parenteral administration of antibiotics, is probably the best treatment.

Four methods with local penicillin therapy are considered. Florey and Williams[17] suggest the drainage of pus by a lateral incision. Daily, the wound is covered with calcium salt of penicillin and packed with gauze soaked with penicillin paste until cultures are negative. The results in 11 cases were optimum in 5, fair in 4 and poor in 2.

Burt[18] advises lateral incisions over the proximal and middle phalanges, and the insertion of two fine-rubber catheters into the tendon sheaths. Penicillin solution is injected through the tubes every three hours for five days. His results in 3 cases were optimum, fair and poor in 1 each.

Marsden[19] recommends the use of two small transverse incisions into the tendon sheath, one just proximal to the metacarpophalangeal crease and the other just proximal to the distal interphalangeal crease. Needles are inserted daily, and penicillin is injected locally; 15,000 units of penicillin is injected every three hours. He reports on 10 cases, with optimum results in 5, fair results in 3 and poor results in 2.

Unonius[20] makes a small, curved incision into the sheath and introduces ureteral catheters proximally and distally. Penicillin solution is injected every six hours until the fluid contains no bacteria. In 8 cases, Unonius reports the following results: optimum in 5, fair in 2 and poor in 1.

Excision with suture technic has recently been suggested for the treatment of suppurative tenosynovitis and deep-fascial-space infection.[21] All slough and necrotic tissue are excised, and the wound is sutured. Local and parenteral administration of penicillin is recommended.

Loudon et al.[10] suggest a transverse incision over the distal end of the sheath. A needle is inserted proximally, and, at times, an incision is made proximally. Ten thousand units of penicillin is injected through the needle, and the incisions are sutured; 20,000 units of sodium penicillin is injected intramuscularly twice a day for five days postoperatively. The results in 7 cases were optimum in 5, fair in none and poor in 2. The authors also recommend this treatment for deep-fascial-space infection.

The parenteral administration of penicillin is more logical than the local use. With adequate circulation in the involved part, the concentration of penicillin in the blood stream may be kept at the proper level to control the infection. With adequate circulation and only local use of penicillin, all recesses of the infection may not be reached. With inadequate circulation in the infected part, neither parenteral nor local administration of penicillin will prevent a poor result.

I have used excision with suture technic in only 1 case of subcuticular abscess, with a poor result.

A wide incision and drainage of the involved tendon sheath, local irrigation of pus and slough and large intramuscular doses of penicillin are preferred. A pneumatic cuff is applied, and a longitudinal incision is made over the medial or lateral aspect of a finger from the base of the proximal phalanx to the base of the distal phalanx. A 1.5-cm. longitudinal palmar incision is made to drain the entire palmar aspect of the sheath. All slough is removed. The opened tendon sheath is irrigated from the proximal end with saline solution; 100,000 units of penicillin in 5 cc. of saline solution is injected into the proximal end of the tendon sheath. A rubber tissue drain may be used for twenty-four to forty-eight hours to separate skin edges only.

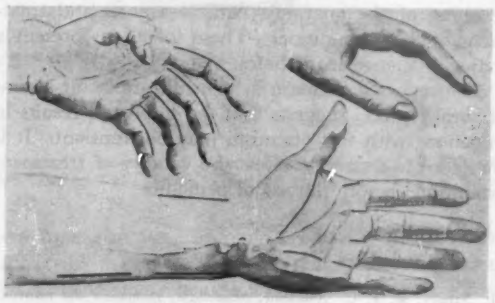

FIGURE 6. *Incisions for Draining Infected Tendon Sheaths, Radial and Ulnar Bursas and Spaces in the Wrist and Forearm.*

Figure 6 shows incisions for tendon-sheath and bursa infections. Postoperatively, the hand is elevated and immobilized in an aluminum splint in a position of function until the infection subsides. Hot fomentations, whose value has been debated in the medical literature, help to decrease any cellulitis that is present; 100,000 units of penicillin is given intravenously immediately after operation and followed by 100,000 units given intramuscularly every three hours until infection subsides, when active motions are begun. My experience in 75 cases, over a ten-year period, indicates about the following results: 68 per cent optimum, 16 per cent fair and 16 per cent poor.

CONCLUSIONS

Three changes in major infections of the hand have been noted since the advent of antibiotics. The frequency has decreased. The complications are less in severity and fewer in number. The results are about twice as good as those before antibiotics were used. The lower prevalence is due to better knowledge, adequate working facilities, improved first aid and definitive treatment, besides antibiotics.

Lymphangitis is about 20 per cent, deep-fascial-space infection about 20 per cent and acute suppurative tenosynovitis about 25 per cent as frequent as they were before antibiotics were introduced at the Boston City Hospital.

The complications of lymphangitis and deep-fascial-space abscess are very rare. The complications of acute suppurative tenosynovitis are less severe and occur about 16 per cent as frequently as they did before the introduction of antibiotics.

The results in the treatment of lymphangitis and deep-fascial-space abscess have improved greatly. Those in acute suppurative tenosynovitis are about twice as good as they were before antibiotics were used.

The decrease in prevalence and the better results with major hand infections since the advent of antibiotics constitute no reason for decreasing study and teaching of the anatomy, clinical aspects and treatment of these conditions. These infections present a major challenge in diabetes.

The reported increase in penicillin-resistant strains of staphylococci suggests that the improved results in infections with this organism may be transient. It is therefore necessary to stress the validity of treatment established before the use of penicillin.

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USE OF RADIOACTIVE POTASSIUM (K^{42}) IN THE STUDY OF BENIGN AND MALIGNANT BREAST TUMORS*

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RADIOACTIVE phosphorus (P^{32}) has been used for the study of human breast tumors by Low-Beer et al.,[1-3] who first reported in 1946 that ulcerating carcinoma of the breast, counted externally in vivo after administration of radioactive phosphate intravenously, showed a significant increase in radioactivity when compared with the normal breast. Benign inflammatory lesions also caused a considerable increase in uptake of P^{32}. Lesions deeper than 0.5 cm. from the surface and mucoid carcinomas at any depth produced no increase in counting rate. The method was therefore limited by a huge uptake of P^{32} in inflamed tissues and by the short range of the beta particles of P^{32} (approximately 0.7 cm.) in the body. Selverstone, Sweet and Ireton[4,5] reported that radioactive potassium localized in high concentration in a number of human cerebral tumors in comparison with normal brain tissue. This difference could be demonstrated not only in tissue samples but also by external counting over the surface of the head. Radioactive potassium (K^{42}) emits, in addition to its beta particles, a gamma ray of high intensity, 1.5 mev., with a half-tissue thickness of approximately 30 cm.¶

Because of this greater penetration, K^{42}, if concentrated by carcinoma of the breast, would offer obvious advantages over P^{32} for detection of tumors deeper than 0.7 cm. The pertinent physical characteristics of the two isotopes are listed in Table 1.

Methods

Radioactive potassium (K^{42}) is obtained as potassium carbonate K_2CO_3 from the Brookhaven National Laboratories. The target material, 11 gm. of K_2CO_3, is irradiated in the nuclear reactor, providing an activity of approximately 130 mc. The target material is dissolved in dilute hydrochloric acid to yield a solution containing 0.044 milliequiv. of potassium ion per cubic centimeter at pH 7.4. The solution is then transferred

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¶Half-tissue thickness is defined as the amount of tissue that reduces the number of original particles per unit area by 50 per cent.

to vaccine vials and autoclaved. Each patient receives an intravenous injection of 0.25 to 0.75 mc. of K^{42}. When we have used a potassium solution of low specific activity, it has been necessary at times to inject 15 to 20 cc. of the solution. Under these circumstances pain sometimes extended up the arm along the course of the vein as far as the shoulder. We have considered this pain to be of local origin in association with a transient high concentration of potassium ion within the vein. This symptom can be controlled by interruption of the injection for about thirty seconds, followed by completion at a slower rate. A continuous electrocardiogram was recorded during a rapid and painful injection in 1 patient. No abnormality was seen before, during or after the injection. More recently K^{42} of higher specific activity has been obtainable; solutions of this material have produced no symptoms during injection.

Since the radioactive potassium is distributed throughout the body, both in the extracellular compartment and within the cells, effective shielding is necessary if a local lesion is to be counted. A direc-

TABLE 1. *Pertinent Physical Characteristics of Radioactive Potassium and Phosphorus.*

ISOTOPE	HALF LIFE	EMISSIONS	MAXIMUM TISSUE PENETRATION
			cm.
Radioactive potassium	12.4 hr.	Gamma & beta rays	>30.0
Radioactive phosphorus	14.3 days	Pure beta rays	0.7

tional effect is obtained by collimation of the gamma beam by means of a lead cylinder, 14 cm. in outside diameter, with an aperture of 3.0 cm. The crystal is recessed 18.2 cm. within the cylinder, which has a total length of 37.5 cm. We are now using a 1.0-cm. cube of thallium-activated sodium iodide closely applied to a photomultiplier tube (RCA No. 5819) (Fig. 1). Standard preamplifier, discriminator and scaling circuits are used. The background averages 50 to 80 counts per minute.

The aperture of the counter shield is apposed to the breast, and counts recorded for one minute. Various positions of the counter in relation to the breast have been tried, the two breasts always being counted in symmetrical fashion. One reduces the radiation from the rest of the body by placing the aperture of the shield in contact with the lateral surface of each breast. The long axis of the shield is horizontal and parallel to the coronal plane of the body. In lesions located in a medial quadrant of the breast, however, we have placed the aperture of the shield in this region. Various intervals between injection and counting have been used to determine the most effective interval for maximal differences between cancerous and normal breasts. Counts made at intervals of one minute to eight hours after injection in various cases showed that the differentiation between carcinomatous and normal breasts was most marked five to fifteen minutes after injection of the isotope. The differential decreases slightly until one hour has elapsed and then falls more rapidly. We therefore routinely begin counting five minutes after administration of the isotope and continue at intervals of two minutes for thirty minutes. The two breasts are counted alternately throughout the period of observation.

Benign and malignant tumors of the breast have been studied in 102 patients, with histologic verifica-

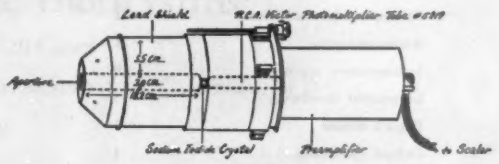

FIGURE 1. *Diagram of a Lead Shield Mounted on a Modified X-Ray-Tube Stand Used to Collimate Gamma Rays.*

tion in each case. The tumors varied in gross size from 5 by 5 mm. to 20 by 15 cm. Table 2 classifies the 38 consecutive benign lesions of this series. Fibroadenoma and chronic cystic mastitis were the most common diagnoses. Cystosarcoma phylloides in 1 case has been arbitrarily assigned to the benign group. Four patients with inflammatory masses from 2.5 to 10 cm. in diameter in one breast were studied. We were able to observe the inflammatory lesions until the process was at its height before undertaking the

TABLE 2. *Classification of Benign Tumors.*

CLASSIFICATION	NO. OF CASES
Chronic cystic mastitis	12
Fibroadenoma	10
Acute abscess	4
Gynecomastia	3
Intraductal papilloma	3
Intraductal hyperplasia	4
Cystosarcoma phylloides	1
Fat necrosis	1
Total	38

K^{42} study. In none of these 4 patients was a significant increase in counting rate noted.

Table 3 lists the 66 consecutive malignant tumors that we have studied. "Inflammatory carcinoma" is considered to be a diffuse cancer without a delineable mass and with erythematous changes overlying the involved area. Pathological examination showed invasion of superficial lymphatic channels in all cases.

Figure 2 presents the "percentage difference" in counting rates between the involved and the normal breast. This mathematical expression, suggested by Low-Beer,[3] is calculated as follows:

$$\text{Percentage difference} = \frac{100 \times \text{counts over tumor} - \text{counts over normal breast}}{\text{counts over normal breast} - \text{body background}}$$

Fifty-two of the 65 patients with malignant tumors showed differences in excess of 20 per cent. No breast containing a benign tumor assayed more than 20 per cent above the normal breast, and in only 3 cases was the discrepancy greater than 10 per cent. In patients with benign tumors the control breast was about as likely to show a higher counting rate as the abnormal breast (Fig. 2).

TABLE 3. *Classification of Malignant Tumors.*

CLASSIFICATION	NO. OF CASES
Scirrhous adenocarcinoma	21
Adenocarcinoma	21
Inflammatory carcinoma	2
Intraductal carcinoma	3
Paget's disease	1
Colloid carcinoma	1
Undifferentiated carcinoma	16
Total	65

Table 4 lists the 13 malignant tumors that showed percentage differences within the range of benign tumors. Ten of these were less than 1.5 cm. in diameter. Two large mucoid carcinomas also lay within the benign range, a finding similar to that of Low-Beer[3] in studies with P^{32}. In general, large tumors showed greater percentage differences than smaller ones. Statistical analysis did not indicate significant differences between tumors classified in Grades 3 and 4 as compared with those in Grades 1 and 2. The presence of lymph-node metastases did not affect the percentage difference in counting rates. The four inflammatory lesions showed differences below 10 per cent, in striking contrast to the high uptake of radioactive phosphorus reported by Low-Beer[3] in such lesions.

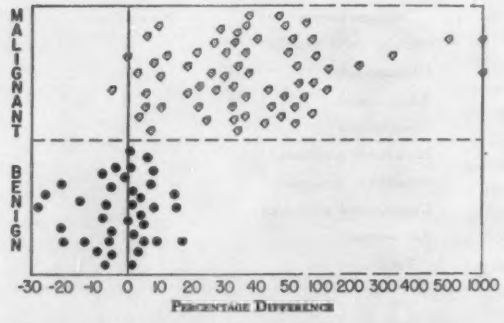

FIGURE 2. *Uptake of Radioactive Potassium in Breast Tumors.*

DISCUSSION

More labeled potassium appears to enter the carcinomatous breast than the normal when the radioactive potassium ion is injected into the blood stream. The benign lesions of the breast that were studied did not share this property. It seems likely that the more rapid metabolism of the malignant neoplastic cells is responsible for this more rapid uptake of labeled potassium. Other explanations for an increased surface counting rate have been considered. The tumor might, because of increased vascularity, contain more K^{42} than normal. However, when radioactive sodium (Na^{24}) was injected intravenously in 2 consecutive patients with unilateral carcinoma of the breast, counts were symmetrical in the two sides. When radioactive potassium was given to the same patients a difference of 30 per cent was found in one and of 35 per cent in the other. It is also possible that tumor tissue contains more exchangeable potassium simply because of its increased cellularity. Benign tumors of comparable size and cellular density, however, did not show increased accumulations of K^{42} in this series. Assay of activity of excised benign tumors does, in fact, show increase in radioactivity, but these are apparently too small to be demonstrated by the crude technic of surface counting.

TABLE 4. *Malignant Tumors (Showing Differences) Similar to Benign Fibroadenomas.*

CLASSIFICATION	NO. OF CASES
Paget's disease	1
Mucoid adenocarcinoma	1
Adenocarcinoma (less than 2 cm.)	5
Undifferentiated carcinoma (less than 2 cm.)	2
Intraductal carcinoma	2
Adenocarcinoma of breast in males	2
Total	13

SUMMARY AND CONCLUSIONS

Radioactive potassium (K^{42}) was administered intravenously to 102 patients with benign and malignant lesions of one breast, and external counts were made in vivo. Malignant tumors increased the local counting rates more than 20 per cent in 53 of 66 cases (80 per cent). No patient with a benign breast lesion showed an increase in counting rate greater than 20 per cent. Since 13 patients with malignant tumors had counting rates within the range of benign tumors, this procedure is not considered to be a diagnostic test.

A positive difference of 20 per cent or more appears to offer presumptive evidence that a mass in one breast is malignant. In no case, however, should surgical treatment be withheld because of failure to demonstrate a significant counting difference. The increased metabolic activity of malignant tumors may

be responsible for the increased counting rates observed.

We are greatly indebted to Miss Ilse M. Pfaltz, Mrs. Mildred Moulton and Mrs. Marcia Holder for their technical assistance and to Miss M. Ruth Hall for preparing the manuscript.

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ACUTE AND CHRONIC CHOLECYSTITIS

A Review of 329 Cases

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BOSTON

THREE hundred and forty-two patients with a preoperative diagnosis of cholecystitis were operated on at the Boston City Hospital from January 1, 1951, to January 1, 1953. The records of 13 cases were not available for study; therefore, 96.2 per cent of the records of the entire group have been reviewed. The series comprised 99 cases with a preoperative diagnosis of acute cholecystitis and 230 cases with a preoperative diagnosis of chronic cholecystitis.

Sex Prevalence

Acute cholecystitis appeared one and a half times more frequently in females whereas chronic cholecystitis appeared five times more frequently in females. Although it was a major factor in the chronic form of the disease, sex does not appear to have had any important effect on the frequency of the acute form of the disease in this series.

Age Prevalence

It is of interest that the peak incidence of cholecystectomy for the chronic form of the disease occurred in the fifth decade of life. In contrast, surgery was performed for acute cholecystitis most frequently on patients in the sixth decade. In general (Fig. 1) the frequency of acute cholecystitis lagged behind that of the chronic form for each decade until the peak prevalence was reached; it was then maintained at a higher level throughout the remaining decades.

Diagnostic Error

Of 99 patients with a preoperative diagnosis of acute cholecystitis, 11 had no disease of the gall bladder. Thus, the diagnostic error for the acute form was 11.1 per cent. The correct diagnoses for these 11 cases were as follows: acute appendicitis, 4 cases; perforated peptic ulcer, 3 cases; marginal ulcer, 1 case; obstructing duodenal ulcer, 1 case; pyelonephritis, 1 case; and pelvic abscess, 1 case.

Of 230 cases with a preoperative diagnosis of chronic cholecystitis, there was no disease of the gall bladder in 22. Therefore, the diagnostic error for the chronic form was 9.6 per cent. The correct diagnoses for these 22 cases were regional ileitis, active duodenal ulcer, fatty nutritional cirrhosis, duodenitis and mucous colitis in 1 case each, and no demonstrable disease in 17 cases. Nine of these 17 patients had a positive Graham series preoperatively; in 1 with a normal Graham series operation was performed on the basis of clinical findings; 7 patients were operated on without a strong history of gall-bladder disease and without a preoperative Graham series.

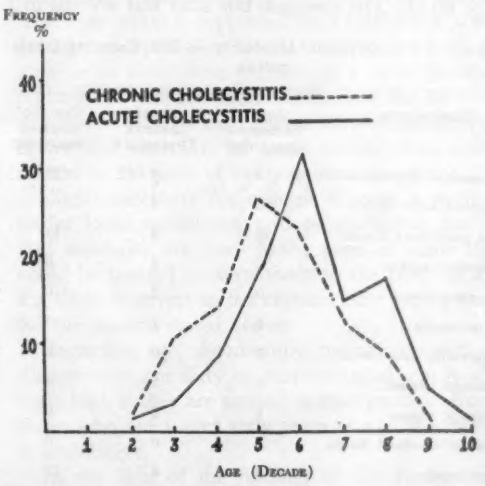

Figure 1. *Age Distribution of 208 Cases of Chronic and 88 Cases of Acute Cholecystitis.*

The diagnostic error of x-ray diagnosis in 184 patients with chronic cholecystitis who had a preoperative Graham series was 4.9 per cent. The diagnosis of

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a diseased gall bladder or cholelithiasis was made in 33 patients on examination of scout films of the abdomen or intravenous pyelograms or at previous laparotomy.

Common-Duct Exploration

The common bile duct was explored in 44 cases of chronic and 20 cases of acute cholecystitis. A positive yield of stones, gravel or mud was obtained in 43.2 per cent of the chronic and 30.0 per cent of the acute cases (Table 1).

Table 1. *Results of Common-Duct Exploration.*

Type of Cholecystitis	Cases Explored	Positive Yield
		No. of Cases
Chronic	44(21.2%)	19(43.2%)
Acute	20(22.7%)	6(30.0%)

Technical Errors

Four serious technical errors were committed in the entire series. The common bile duct was severed in 1 case and injured in another. In 2 cases a serious hemorrhage from the cystic-artery stump occurred during the procedure.

Table 2. *Postoperative Morbidity in 296 Cases of Cholecystitis.*

Complication	Acute Emergency Operation*	Acute Elective Operation†	Chronic Elective Operation‡
Postoperative hypotension	4	4	22
Congestive heart failure	2	1	0
Acute pulmonary disease	10	4	13
Respiratory acidosis	2	0	0
Pulmonary abscess	0	1	0
Bile peritonitis	1	1	0
Postoperative pancreatitis	0	0	0
Subphrenic abscess	1	1	0
Subhepatic abscess	1	0	0
Cutaneous duodenal fistula	1	0	0
Wound sepsis	9	8	12
Incisional hematoma	0	1	1
Wound dehiscence	1	0	2
Phlebothrombosis	1	1	0
Totals	33	22	50

*36 cases.
†52 cases.
‡208 cases.

Postoperative Morbidity

All significant postoperative complications are listed in Table 2. Complications are presented under three classifications to emphasize the high morbidity that follows gall-bladder surgery performed on an emergency basis. The term "emergency" means that the patient was operated on within twenty hours of admission and without the delay entailed by an elective operating schedule. Of the 36 patients in the emergency acute group, 21 had 33 complications; of the 52 patients in the elective acute group, 22 had 22 complications. This marked difference is in part due to the fact that the more seriously ill patients were operated on as emergencies. However, this fact applies to only a few patients in the emergency group and only partially explains the much greater frequency of complications among such cases. This is better understood when it is explained that many of the staff members believe that most cases of acute cholecystitis should be treated as emergencies. Of the 208 patients with chronic cholecystitis, 43 had 50 complications. Expressed in another way, there was a case complication rate of 58.3 per cent for the acute emergency, 42.3 per cent for the acute elective and 20.7 per cent for the chronic cases.

Table 3. *Mortality in 296 Cases of Cholecystitis.*

Type of Case	No. of Cases	No. of Deaths	Mortality
			%
Acute (emergency operation)	36	5	13.9
In patients over 60	13	3	23.1
In patients under 60	23	2	8.7
Acute (elective operation)	52	2	3.9
In patients over 60	21	2	9.5
In patients under 60	31	0	—
Totals	88	7	
Average			7.9
Chronic in patients over 60	44	3	6.8
Chronic in patients under 60	164	1	0.6
Totals	208	4	
Average			1.9

Mortality

The mortality for 88 cases of acute cholecystitis in this study was 7.9 per cent. The mortality for the 36 cases of acute cholecystitis requiring emergency operations was 13.0 per cent. That for the 52 acute cases requiring elective procedures was 3.9 per cent. The mortality for 208 cases of chronic cholecystitis was 1.9 per cent. In Table 3 these groups are further subdivided to present rates for patients who were less than sixty years of age or sixty or more years of age. In the entire series there were 13 patients with diabetes mellitus; only 1 of these patients died.

Perforated Gall Bladder

A grossly evident perforation of the gall bladder was found in 13 cases of acute cholecystitis, making the rate of perforation in this series 14.7 per cent.

There was only 1 death in this small group, which contained 6 patients over seventy-three years of age, the oldest being seventy-nine years of age. Six patients with perforated gall bladders were in the acute group with emergency operations, and 7 in the acute group with elective procedures; only 1 patient of the latter had sufficient change in symptoms to warrant a belief that the gall bladder had perforated after admission to the hospital.

Palpable Gall Bladders

The gall bladder was palpable in 28 acute cases, the rate being equally divided between the patients with emergency and those with elective operations. Seven patients, or 50 per cent, of each group had complications. There were 3 deaths among the patients with palpable gall bladders subjected to emergency procedures and only 1 among those who underwent elective operations.

Pancreatitis and Peptic Ulcer

A history of one or more verified attacks of pancreatitis was elicited from 15 patients with chronic cholecystitis. Two patients with acute cholecystitis had acute pancreatitis at the time of operation. In 2 cases of pancreatitis both cholelithiasis and choledocholithiasis were found. One patient with chronic cholecystitis had choledocholithiasis, pancreatitis and a spontaneous cholecystoduodenal fistula. Twenty patients had active duodenal ulcers or evidence of healed duodenal ulcers; 3 had gastric ulcers.

Unusual Pathological Findings

Interesting pathological findings in this study were as follows: cystic-duct remnant containing gravel (1 case); dilated cystic-duct remnant with common-duct stone (1 case); spontaneous cholecystogastric fistula (1 case); spontaneous cholecystoduodenal fistula with stone in the common duct (1 case); spontaneous cholecystoduodenal fistula with a mud cast in the common duct (1 case); diverticulum of the gall bladder (1 case); mucous polyp of the gall bladder (1 case); incidental finding of an epidermoid carcinoma of the gall bladder (1 case); adenocarcinoma of the gall bladder associated with acute cholecystitis (1 case).

Discussion

The material presented in this study emphasizes the need for a more conservative approach to the treatment of acute cholecystitis. Although cholecystectomy in the acute form of the disease challenges the technical ability of the surgeon, there is no doubt that the patient is subjected to a real increase in morbidity and mortality when the procedure is undertaken as an emergency. So far as the patient's welfare is concerned it is far better to allow adequate preparation, even in the presence of progressive symptoms, and to delay surgery in cases that are clinically stabilized or subsiding.

The refusal of the surgeon to delay operation during the acute phase for the reason that patients frequently avoid cholecystectomy when they are feeling well again can be refuted by the statement that most of these patients later refuse cholecystectomy because of inadequate follow-up efforts on the part of the surgeon. The surgeon is obligated to make his patient fully aware of the morbid consequences of the disease. He should not hesitate to recommend what he considers the best possible treatment for cholecystitis.

There is no reason for the surgeon to be unduly alarmed when he is confronted with a palpable or perforated gall bladder. It is a well known fact that spillage from a perforation will almost always be walled off by surrounding structures in the right upper quadrant. The only perforated gall bladder that led to death in this series occurred in the emergency group. We regard this as a significant finding.

We believe that a palpable, tender gall bladder is not in itself an indication for immediate operation. This contention is supported by 3 fatal cases in which emergency operations were performed. It is more sensible to place these patients on a strict therapeutic regimen to prepare them adequately for an elective procedure. Such a plan lowers the postoperative morbidity and mortality of acute cholecystitis, and this should be the goal of every general surgeon.

Cholecystectomy for chronic disease is performed under ideal conditions, and postoperative morbidity and mortality are low. Many cases of acute disease could be treated conservatively to the point of allowing them to revert to the chronic state before surgery, for the reasons stated above.

Regarding age, the mortality for patients with acute disease who are sixty or more years of age is alarmingly high if they are treated as emergencies. Even for those who are under sixty years of age the mortality is prohibitive.

In the light of the findings of this study it is believed that the acute gall bladder should not be treated surgically without an adequate period of preparation.

Summary

A review of 230 cases with a preoperative diagnosis of chronic cholecystitis and 99 cases with a preoperative diagnosis of acute cholecystitis is presented.

The alarmingly high morbidity and mortality associated with the emergency treatment of acute cholecystitis and the need for a more conservative approach are stressed.

THE VITAL CAPACITY AS A MEASURE OF THE SPONTANEOUS BREATHING ABILITY IN POLIOMYELITIS*

B. G. FERRIS, JR., M.D.,† A. WARREN‡ AND C. A. BEALS‡

BOSTON

THERE has long been a need for a simple objective criterion to indicate when use of a respirator should be started during the acute illness of poliomyelitis and to guide the weaning of patients with respiratory-muscle paralysis from respirators. Some authors[1,2] have used the vital capacity during the acute illness to indicate when patients should be placed in a respirator. They presented no objective data for the statement that patients should be placed in tank respirators when the vital capacity was 25 per cent of the predicted value. Affeldt[3] measured the vital capacity at intervals during periods of unassisted breathing in long-term-convalescent patients with poliomyelitis; if he observed a fall in the measurement during continuous unassisted breathing, he reasoned that respiratory-muscle "fatigue" was present. Affeldt did not develop a specific relation between the unassisted time and the vital capacity as a percentage of the predicted vital capacity. Since the vital capacity is a well accepted measurement and relatively easy to perform, the present study was undertaken to obtain data that might have a bearing on the optimum time when paralyzed patients should be placed in tank respirators during the acute illness of poliomyelitis. In addition, it was believed that Affeldt's observations could be extended so that only one short series of measurements of the vital capacity would suffice to predict a safe period of unassisted breathing for paralyzed patients during convalescence.

TABLE 1. *Vital-Capacity Tolerance Test in E. S., a Twenty-six-Year-Old Patient.*

TIME	VITAL CAPACITY*	RESPIRATIONS	PULSE	BLOOD PRESSURE	REMARKS
	liter	*per min.*	*per min.*	*mm. Hg.*	
7:30 a.m. (start)	0.53				Patient off rocking bed
10:10	0.53	24	120	122/88	Patient supine
10:25	0.49	20	96	120/76	Patient supine
10:45	0.49	20	112	120/78	Patient supine
11:00	0.48	20	96	118/80	Patient supine
11:15	0.49	24	88	116/78	Physical examination
11:45†	0.48	24	96	122/84	Foot soak
12:15 p.m.	0.45	24	88	120/80	Bath
12:45	0.41	20	112	116/86	Patient feeding self (sitting up 35°)
1:15 (end)	0.41	20	120	122/86	Patient supine (after meal)

*Corrected to body temperature & ambient pressure & saturated with water vapor.

†Patient's maximum unassisted-breathing time for any one period set at 4¼ hr. on basis of subsequently sustained fall in vital capacity.

METHOD

Vital capacities were measured with the patient in the supine position. A recording spirometer with valves and soda lime absorber removed§ or a modified dry gas meter¶ was used. All volumes were corrected to body temperature and ambient pressure and saturated with water vapor. Vital-capacity values for adults were predicted from the regression equations of Baldwin et al.,[4] and those for children and adolescents (five to sixteen years of age) from the data of Ferris and his associates.[5,6] In children

TABLE 2. *Vital-Capacity Tolerance Test in R. Wa., a Twenty-nine-Year-Old Woman.*

TIME	VITAL CAPACITY*	PULSE	RESPIRATIONS	BLOOD PRESSURE	REMARKS
	liter	*per min.*	*per min.*	*mm. Hg.*	
10:00 a.m. (start)					Patient out of tank respirator & onto bed
10:15	0.54	88	24	126/64	Patient in bath
11:30	0.53	92	20	106/64	Patient back from hydrotherapy
12:30 p.m.	0.48	88	24	122/65	After lunch
1:00	0.55	84	20	114/76	Patient reading
1:20	0.53	80	24	110/70	Patient reading
1:40	0.52	—	—	—	Hot packs
2:00	0.54	96	—	—	Hot packs
2:20	0.50	80	24	108/64	Patient out of packs
2:40	0.48	92	24	106/78	Patient reading
3:00	0.50	96	24	110/75	Patient talking with social-service worker
3:20†	0.51	96	24	110/72	Patient reading
3:40	0.46	84	20	108/68	Patient reading
4:00	0.44	84	24	112/78	Physiotherapy
4:20 (end)	0.43	92	20	112/80	Patient reading

*Corrected to body temperature & ambient pressure & saturated with water vapor.

†Patient's maximum unassisted-breathing time set at 5½ hr. for any one period on basis of subsequently sustained fall in vital capacity.

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Aided by a grant from the National Foundation for Infantile Paralysis, Incorporated.

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§Collins Vitalometer and Ventilometer, available from W. H. Collins Company, Boston.

¶Emerson Breathometer, available from J. H. Emerson Company, Cambridge, Massachusetts.

under five years predicted values were approximated by extrapolation of the curves obtained on older children.

Patients with respiratory-muscle paralysis due to poliomyelitis were studied in the acute and in the convalescent stages. In 56 convalescent patients the optimum unassisted time was determined by measurement of the vital capacity at regular intervals during a period of continuous unassisted breathing. All the chronically ill patients had performed the vital-capacity test repeatedly and could be considered trained subjects except for the 2 young children under five years of age. The appearance of a sustained fall of 15 to 20 per cent in the observed vital capacity was taken to represent the onset of "fatigue" of the functioning respiratory muscles. Repeated measurements of the vital capacity in this manner will be referred to as the "vital-capacity tolerance test." The optimum unassisted breathing time or the breathing time without "fatigue" was considered to be the interval before such a sustained fall in the vital capacity. It was noted in the early application of this test that some adult patients with extremely low vital capacities (200 to 400 cc.) showed no fall in vital capacity but did manifest tachycardia, tachypnea and flushed faces. This observation suggested that some patients could master

TABLE 3. *Serial Vital-Capacity Measurements and Unassisted-Breathing Times in Patients Convalescing from Poliomyelitis.*

PATIENT	SEX	AGE	PREDICTED VITAL CAPACITY	DATE OBSERVED	OBSERVED VITAL CAPACITY*	VITAL CAPACITY†	CONTINUOUS UNASSISTED-BREATHING TIME
		yr.	*liters*		*liters*	*%*	*hr.*
T.C.	M	29	4.73	12/2/52	0.83	17.5	5.5
				12/15/52	1.22	25.8	13.5
				2/5/53	1.28	27.2	16.5
				3/18/53	1.52	32.2	20.0
				6/19/53	1.82	38.5	84.0
M.H.	F	24	3.29	2/25/53	0.16	5.0	0.05
				11/20/53	0.32	9.9	1.5
R.Wa.	F	29	2.96	10/13/53	0.42	13.9	0.5
				11/3/53	0.60	22.3	3.2
				11/10/53	0.54	18.2	5.5
				1/3/54	0.75	25.3	5.5
F.E.	M	32	4.27	12/8/52	0.40	9.5	0.5
				11/9/53	0.54	12.6	11.0

*Corrected to body temperature & ambient pressure & saturated with water vapor.

† $\frac{\text{Observed}}{\text{Predicted}} \times 100$.

enough strength for a single vital-capacity test but were unable to provide adequate alveolar ventilation during prolonged unassisted breathing. Subsequently, the pulse and respiratory rate were counted for a minute interval, and the blood pressure was measured by means of auscultation with a sphygmomanometer; an increase of 15 to 20 per cent in any of these parameters was taken as an early sign of ventilatory insufficiency with probable carbon dioxide retention, and the test was stopped. In patients with larger vital capacities the pulse and respiratory rates were less useful since emotional factors were often present and produced much variability. Three patients acutely ill with varying degrees of respiratory-muscle paralysis due to poliomyelitis were also included. Their vital capacities were recorded, and the longest duration of unassisted breathing at one

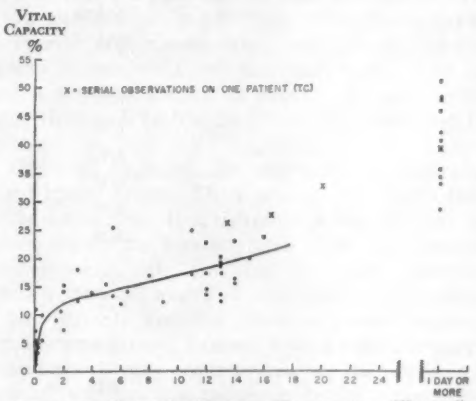

FIGURE 1. *Relation of Vital Capacity* $\left(\frac{Observed}{Predicted} X\ 100\right)$ *and Unassisted-Breathing Time in Patients Convalescing from Poliomyelitis.*

interval was recorded. "Unassisted-breathing time" was determined by the patients' subjective sensations, by the clinical judgment of the resident staff and by the observations of clinical signs such as increased pulse and respiratory rate, dilatation of the alae nasi, use of accessory muscles of respiration and flushing of the skin. In no patient was visible cyanosis allowed to develop. No "vital-capacity tolerance tests" were done on the acutely ill subjects.

RESULTS

Examples of "vital-capacity tolerance tests" on 2 patients are presented in Tables 1 and 2. Patient E. S. demonstrates the lability of pulse and respiratory rate that was occasionally noted. Since the ventilatory requirements are largely determined by the carbon dioxide production, a record was maintained of the patient's activity during the period of continuous unassisted breathing; the period during which the vital capacity remained at the control level then gave a measurement of the patient's optimum unassisted-breathing time at that level of activity. The results of such studies on convalescent patients are shown graphically in Figure 1, in which the initial vital capacity as a percentage of the predicted vital capacity for that patient is plotted against the

continuous unassisted-breathing time without "fatigue" of the same patient. In patients with severe respiratory-muscle paralysis a minimal value for the vital capacity as a percentage of the predicted value apparently must be present before unassisted breathing can be maintained for one or two hours. This value is about 10 per cent of the predicted values used in this study. The unassisted-breathing time can be improved greatly with only slight absolute increases in the vital capacity. This rise in vital capacity, however, represents a 100 per cent increase over the initial value. In addition, there seemed to be another minimal value of the vital capacity before a patient may be expected to breathe for twenty-four hours or more unassisted; in this group of patients this value appeared to lie between 30 and 35 per cent of the predicted value. None of these patients performed glossopharyngeal breathing. Those who can do glossopharyngeal breathing probably would be able to breathe for a longer period than would be expected from their vital capacity.

TABLE 4. *Serial Vital-Capacity Measurements and Unassisted-Breathing Times in Patients Acutely Ill with Poliomyelitis.*

PATIENT	SEX	AGE	PREDICTED VITAL CAPACITY	DATE OBSERVED	OBSERVED VITAL CAPACITY*	VITAL CAPACITY†	CONTINUOUS UNASSISTED-BREATHING TIME	REMARKS
		yr.	*liters*		*liters*	%	*hr.*	
B.T.	F	24	3.24	7/17/53	0.70	21.6	0.2	Patient febrile
				7/18	0.43	13.3	0.02	Patient febrile
				7/20	0.40	12.4	0.2	Patient afebrile
				7/21	0.48	14.8	0.2	Patient afebrile
				7/24	0.70	21.6	0.33	
				8/8	0.90	27.8	13.0	
				8/18	1.05	32.4	18.0	
				8/20	1.20	37.1	24.0	
				8/26	1.20	37.1	(Continuously unassisted)	
				9/8	1.20	37.1		
				10/2	1.70	52.5		
J.C.	M	6	1.93	9/18/53	0.50	25.9	0.1	Patient acutely ill & dyspneic
				9/25	0.50	25.9	5.0	
				9/27	0.40	20.7	5.5	Patient afebrile
				10/2	0.38	19.5	8.0	Patient afebrile
				10/10	0.85	44.0	11.0	Patient afebrile
				10/17	0.90	46.6	21.0	
				11/9			(Continuously unassisted)	
				1/20/54	1.00	51.9	(Continuously unassisted)	
				3/8	1.20	62.2	(Continuously unassisted)	
E.M.	F	16½	3.22	10/2/53	2.0	62.2	>24.0	
				10/4	1.1	34.2	22.0	Patient febrile
				10/5	0.8	25.0	0.5	Patient febrile
				10/6	0.38	11.8	0.5	Patient afebrile
				10/8	0.85	26.4	4.5	Patient afebrile
				10/14	1.1	34.2	23.0	Patient afebrile
				10/19	1.2	37.3	22.5	

*Corrected to body temperature & ambient pressure & saturated with water vapor.

† $\frac{\text{Observed}}{\text{Predicted}} \times 100$.

Some of the patients convalescing from chronic poliomyelitis manifested an increase in vital capacity and unassisted-breathing time during the period of hospitalization. Representative patients of this type are shown in Table 3, and the results obtained in 1 patient (T. C.) are plotted in Figure 1. Patient R. Wa. almost doubled her vital capacity during the three months under observation, but her unassisted-breathing time did not improve as well as would have been predicted. The reasons for this are not clear, but since data are available only for the eight

months elapsing since the onset of illness, a further increase in her unassisted-breathing time commensurate with the increase in her vital capacity may yet occur. In contrast to patient R. Wa., patient F. E. increased his vital capacity only slightly and yet increased his unassisted-breathing time markedly. This man has shown an increasing hematocrit and arterial oxygen unsaturation and a slightly elevated arterial carbon dioxide pressure. He was able to breathe unassisted for as long as eleven hours when sitting up at an angle of 30 to 40°.* He probably represents a person who was chronically underventilated and whose unassisted-breathing time should have been decreased.

Since it was considered inadvisable to subject the acutely ill patients to the "vital capacity tolerance test," the vital capacities were tabulated and the length of time that they were allowed to breathe unassisted recorded. Observations in 3 acutely ill patients are presented in Table 4. It is important to note that in each case the patient spent more time in a tank or chest respirator than would have been expected from the relation of the observed vital capacity expressed as a percentage of the predicted vital capacity and the unassisted time. Many different factors determine this, such as apprehension and fever, with an increased carbon dioxide production. On the basis of their clinical observation the attending physicians believed that the patients needed the respiratory assistance.

Discussion

As a result of these observations on the acutely ill and convalescent patients, certain criteria may be outlined to determine when respiratory assistance should be given during the acute illness. Since the patients with chronic poliomyelitis require a vital capacity of about 30 to 35 per cent of the predicted value before they can breathe unassisted for twenty-four hours or more, and since their carbon dioxide production is less than that of an acutely ill, febrile, apprehensive patient, it is believed that during the acute stage, when the vital capacity falls to 50 per cent of the predicted value or below, the acutely ill patient should be given a trial in a respirator, preferably a tank type. At this time the procedure will not be a life-saving maneuver, and the patient will be more rational; there will be no need to rush; the patient and the attendants will not be so apprehensive; and, most important, the patient can be told that this is only a temporary arrangement and that he will be taken out of the respirator after a short period. After the trial in the tank respirator he should be removed from the respirator at least for a short time. This will reassure him that the tank is merely an aid to his breathing. The early use of a tank respirator will enable the staff to work without apprehension and will permit the patient to gain confidence in the staff and the tank respirator. It will also help to reduce the extreme fear and apprehension that is experienced with the loss of respiratory function. After the acute phase has passed, this procedure has tremendous psychic implications when it is time to start a program of weaning the patient from the tank respirator.

When the vital capacity falls to a third of the predicted value or below, the patient should be in a tank respirator most of the time. This should be done in an effort to rest the respiratory muscles just as an attempt is made to rest other parts of the body when patients are put to bed. If the patient fails to breathe with the machine, and fights it, the procedure is not restful; on the other hand, if he has had a previous chance to become adjusted to the tank, there will be less likelihood of his resisting the machine.

The vital capacity, like any other measurement, is subject to errors. These are usually due to leaks in the apparatus. It is therefore important that the person taking the measurements make sure that the mouthpiece is tight and that the nose is blocked. Another possible source of error is lack of training of the patient. For this reason repeated measurements are necessary. In some cases low vital-capacity measurements may occur because of pain or muscle "spasm" without true paralysis, or there may be a failure of muscle co-ordination. The apparatus used should have a low resistance so that the work required is not unduly great.

*It is interesting that movement of one hemidiaphragm (right, 1 cm.) only occurred when he sat up at this angle.

Conclusions

The vital capacity is a useful index of the need for respiratory aid during the course of poliomyelitis. Expressed as a percentage of the predicted vital capacity it can be used as an index to determine when a patient should be given a trial in a tank respirator and to guide the weaning program. It is recommended that when the vital capacity falls below half the predicted value, the patient should be given a trial in a respirator. The beneficial implications of this are discussed. Furthermore, when the vital capacity is below a third of the predicted value, use of a tank respirator during several hours of the day is indicated. The exact length of time tank respirators or other devices will be required will vary, depending on individual considerations.

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MEDICAL PROGRESS

THE MEDICAL SIGNIFICANCE OF LENTICULAR OPACITIES (CATARACT) BEFORE THE AGE OF FIFTY*

With Emphasis on Their Occurrence in Systemic Disorders

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THE association of presenile lenticular opacities (cataract) with various medical disorders has not received collective attention in the medical literature to date. Much has been written in the ophthalmologic literature in this regard and several excellent sources of information dealing with cataracts and their various classifications are available.[1-6] Sorsby[7] and Tassman[8] have in textbook form each offered a complete treatise on the many ophthalmologic conditions encountered in systemic medical disease, and Igersheimer[9] and more recently Kirby and Danforth[10] have brought the subject of lens anomalies and cataract to the medical practitioner's attention. However, these particular publications do not deal primarily with the association of cataract and the medical conditions themselves. Consequently, it seems worth while to classify and discuss presenile cataracts in relation to their occurrence in various medical disorders, as well as to attempt to assay their diagnostic significance for the practicing physician, who in the final analysis has initial contact with patients presenting this problem.

Accordingly, a medical classification of cataract before the age of fifty is presented in Table 1. An attempt has been made to include all the more important medical conditions in which lenticular opacities are encountered. As can be readily seen from the table there are a large number of clinical situations in which significant lens opacifications are found. Prompt recognition of several of these pathologic states assumes major importance because the opacities are often the result of changes induced by the underlying disorder. Included in the discussion are some thoughts regarding the possible part played by the underlying disease in the genesis of the lenticular changes.

GENERAL CONSIDERATIONS

Cataract to the ophthalmologist connotes *any* opacity in the crystalline lens. On the other hand it seems safe to assume that to most internists the word "cataract" is more sinister and usually implies a quite obvious lenticular opacity that interferes to some degree with vision. It is necessary to accept the ophthalmologist's concept of cataract in a discussion of the medical importance of lenticular opacification for the simple reason that not all *significant* opacities are readily seen nor do they necessarily interfere with vision. The use of mydriatics and the slit lamp may be necessary for visualization of many important lens opacities. In this discussion therefore, the term "cataract" is employed in the broad sense — that is, to mean any opacity of the crystalline lens.

Interestingly enough, even though the lens is ordinarily considered to be a transparent structure, most normal persons in the younger age groups actually have lenticular opacities. In a group of 150 normal subjects between the ages of eighteen and forty, Bellows[11] found on slit-lamp microscopy that all but 8 of the 300 eyes examined (97.3 per cent) had some form of punctate opacity. Likewise, Doggart,[12] in a series of 300 military men averaging twenty-eight and two-tenths years of age, found cataract in 94.3 per cent using only focal illumination and a loupe. The rate increased to 98 per cent when the pupils were dilated and the lenses were examined with the slit lamp. In no case in the series of either Bellows or Doggart did any patient have interference with vision or evidence of an ocular or systemic disorder. All the opacities were considered to be stationary and benign. Cataracts, therefore, are practically a universal finding in the presenile age groups, but this is not particularly disconcerting since qualified ophthalmologists can usually distinguish between insignificant cataracts of this type and those associated with systemic or ocular disease.

The fact that cataract can be seen in most cases by direct or oblique focal illumination and without mydriasis[12] makes it imperative that the practicing physician give proper attention to the lens during physical examination. He can do this by first making sure that the cornea is clear and then, with a standard ophthalmoscope, focusing on the fundus so as to obtain the best possible orange-red reflex. Opacities appear as shadowing or dark spots interrupting the reflex that do not change position on movement of the eye.‡[13] Mydriasis may be necessary to demonstrate peripheral opacities of the lens, and the pupil can be safely dilated by the examiner provided he is certain that glaucoma is not present.[9] It is to be stressed that, when systemic disorders are suspected, complete diagnostic evaluation of the lens will require the com-

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‡Opacities confined to the posterior portion of the lens move to some extent and in a direction opposite to the movement of the eye.

bined efforts of the internist and the well trained ophthalmologist.

For a proper evaluation of the role of underlying disease in the genesis of cataract, especially of the acquired type, knowledge of certain basic facts regarding the normal lens is essential.

TABLE 1. *Medical Classification of Cataract before the Age of Fifty.**

I. CONGENITAL CATARACT (Present at Birth):
- A) True developmental (idiokinetic) defects.
- B) Environmental developmental defects.

II. ACQUIRED CATARACT:
- A) Associated with genetic disorders:
  1) Latent cataractous disorders.
  2) Mongolism.
  3) Werner's and Rothmund's syndromes.
  4) Myotonic dystrophy.
  5) Inborn metabolic errors.
     a. Galactosemia.
     b. Wilson's disease (hepatolenticular degeneration).
     c. Organic aciduria.
- B) Associated with endocrine disorders:
  1) Cretinism and myxedema.
  2) Diabetes mellitus.
  3) Hypoparathyroidism.
     a. Post-thyroidectomy.
     b. Idiopathic.
     c. Pseudoform (Seabright-Bantam).
- C) Associated with hypocalcemia (other than hypoparathyroidism):
  1) Idiopathic steatorrhea (sprue).
  2) Osteomalacia and rickets.
- D) Associated with intraocular disease:
  1) Corneal disease.
  2) Uveal-tract disease.
  3) Other ocular disorders (tumor, retinitis, retinal detachment etc.).
- E) Associated with "aortic-arch" syndromes:
  1) "Pulseless" disease (Takayasu's disease).
- F) Associated with skin disorders:
  1) Atopic dermatitis.
- G) Due to poisons:
  1) Naphthalene.
  2) Dinitrophenol.
  3) Ergot.
- H) Due to physical agents including trauma:
  1) Foreign bodies:
     a. Iron and copper.
     b. Mercury and silver.
  2) Contusive or lacerative injury.
  3) Irradiation:
     a. Ionizing radiation.
     b. Heat.
     c. Electricity and lightning.

*It should be noted that some medical situations in this classification can be encountered in patients over 50. To exclude senile degenerative changes as being casually or causally related to cataracts, age 50 was chosen as assumed limit of normal lens life before significant senile degeneration has begun.

The lens is derived embryologically from ectoderm and is an exceptional organ in that none of its cells formed during development and growth are destroyed or replaced. This cytologic preservation continues during prenatal and throughout postnatal life. The earliest cells are found at the center of the lens, and the later formed fibers are superimposed on these like the layers of an onion, being added continually throughout life but at a progressively slower rate. In the adult lens one can, with the use of the slit lamp, distinguish different zones of optical discontinuity that correspond closely to the various growth phases: *the embryonic nucleus,* formed in the first three months; *the fetal nucleus* (third to eighth month); *the infantile nucleus* (period from birth to puberty) and *the adult nucleus, cortex and lens capsule.* Thus, since the lens is essentially a clear structure, opacities can often be localized in relation to the time of their occurrence, and this may aid considerably in establishing the proper clinical significance of any given cataract.

The lens is also unique in that during postnatal life it has no direct blood supply and must derive its nutrient supply entirely from the intraocular fluid. This avascularity makes inflammatory reaction to pathologic injury impossible so that primary inflammatory processes do not occur. It is essential to realize, therefore, that cataract is usually the result of non-inflammatory disorders that act either directly or indirectly on the lens.

A brief comparative summary of the major constituents of the normal lens and the cataractous lens is presented in Table 2.[1-5] It can be seen that water and protein make up the majority of lens weight and that essential lipids and minerals account for most of the remainder. The changes that occur when a lens becomes cataractous are shown to be an increase in water, lipids, sodium and calcium, with a decrease in protein, potassium and phosphate.

TABLE 2. *Composition of Normal and Cataractous Lenses.*[1-5]

CONSTITUENT	CONTENT IN NORMAL LENS	CONTENT IN CATARACTOUS LENS
Water content	60-65% (wet wt.)	Increased
Protein	30-35% (wet wt.)	Decreased
Essential lipids	1- 2% (wet wt.)	Increased
Minerals (ash)	1- 2% (wet wt.)	Increased
Calcium	< 0.1% (ash)	Markedly increased
Potassium	> 25% (ash)	Markedly decreased
Sodium	< 10% (ash)	Increased
Phosphate	> 1% (ash)	Decreased

In the pathogenesis of cataract the proteins are the most important constituent of the lens. Permanent alteration of the lens protein (coagulation) produces cellular death, with consequent loss of nitrogen, potassium and phosphorus. The ensuing accumulation of acid metabolites lowers lenticular pH — activating proteolytic enzymes that break the protein down to smaller moieties and complete the cellular destruction. Some of the smaller protein moieties (peptides and amino acids) are lost from the lens, but the remaining increased number of smaller particles raise intralenticular osmotic pressure, with consequent influx of water into the lens.[14] If one accepts the concept that alterations of lens protein are of primary importance in cataract formation most of the other changes that are found seem explainable. Cellular death of lens fibers is followed by lenticular acidosis, nitrogen, potassium and phosphate loss and an increase in intralenticular osmolarity with water and sodium diffusing into the lens to readjust this disparity. Lipoid and calcium deposition occur in the degenerated lens fibers, producing the opacity recognized as irreversible cataract.

Knowledge of the exact metabolism of the lens is far from complete, but a few points are worthy of mention. Since it is an avascular organ lenticular oxygen consumption is, as expected, quite low. The lens utilizes glucose as its main source of energy (aerobically and anaerobically) and is liberally supplied with complex autoxidation systems, including a sulfhydril system (cysteine and glutathione), an ascorbic acid system and a lactoflavin (vitamin B_2) system. The integrity of these oxidative systems is critical since cataractous lenses are characterized by a diminished oxygen consumption and a loss of the substances active in oxidation (cysteine, ascorbic acid and so forth). Consequently, cataract may be considered a sign of lenticular asphyxia.[15]

Cataracts must be considered to be usually a result of altered physicochemical processes within the lenticular tissue, and from the foregoing discussion one can appreciate the fact that there are many possible etiologic causes for their formation. Buschke,[6] recognizing this difficulty, proposed a classification based on experimentally produced and clinically encountered cataracts. He separated cataracts into three groups — the *diabetic*, the *tetanic* and the *dystrophic*. The diabetic group included experimental cataract produced by galactose and xylose as well as the clinical diabetic cataract; the main etiologic factor responsible for this type of cataract was postulated to be changes in osmolarity in the intraocular fluid, with secondary water imbibing by the lens. The tetanic group was composed of clinical and experimental hypoparathyroid and hypocalcemic states, and the dystrophic group included the majority of cataracts of the acquired type presented in the second major classification given in Table 1. Buschke postulated that metabolic disturbances either genetically determined or postnatally acquired were responsible for the lenticular changes in the various experimental and clinical situations. He stressed the point that indefinite, meaningless statements such as "cataracts due to endocrine dysfunction or nutritional disturbances" should not be bandied about, and he further suggested that metabolic defects would probably be identified at a later date, accounting for the changes in the lens and other tissues in the various clinical and experimental states. This view still seems most reasonable and points to the importance of continued attempts to define specific metabolic and enzymatic abnormalities that may well be common denominators in various syndromes in which cataract is encountered.

Congenital Cataract

There are a wide variety of cataracts that occur primarily from prenatal developmental defects. These opacities properly considered include only those present *at birth* and exclude all that appear later. Much confusion seems to exist in the literature regarding this point, and "congenital cataracts" often connote those that develop some time in postnatal life. In recent years the identification of specific defects (inborn or acquired metabolic errors) has made it necessary to keep an open mind concerning which genetic abnormalities are truly congenital and which are acquired. It is certainly conceivable, for example, that cataract may not be a primary congenital defect but may be secondary to some disorganization of metabolism occasioned by the primary defect. This, indeed, has been exemplified in recent years by the cataract seen in the syndrome of galactosemia in infants.[16]

True Developmental (Idiokinetic) Defects

Many, if not most, of the cataracts present at birth are the result of true developmental or growth aberrations. They have been adequately described by Cordes[17] in relation to the specific developmental derangements responsible for their formation. The significant lens opacities are usually bilateral, and they are most often stationary after birth. There is frequently a marked heredofamilial tendency, and occasionally consanguinity in the genealogic tree is encountered. Usually, associated congenital defects are present. Falls[18] surveyed 131 cases of congenital cataract and noted associated congenital eye defects in 52.6 per cent, and associated constitutional defects in 29.7 per cent. The constitutional disturbances included mental retardation, congenital heart lesions, spina bifida, club foot, harelip and deafness. These patients were not screened for conditions in the mother that are now known to lead to congenital cataract (such as rubella), and it is probable that some of his patients did not have true idiokinetic lens defects. Other reports have lent support to Falls's basic findings.[19-22]

True developmental cataract has been described as a single genetic defect transmitted as a dominant but not sex-linked characteristic.[23] Examples of this include the so-called "Coppock cataract," originally described by Nettleship and Ogilvie[24] and more recently by Lee and Benedict,[25] in which the fetal nucleus is involved; the disk-shaped cataract, as reported by Haro,[26] in which the lenticular nucleus is absent; and the zonular type,[17] in which only a circumscribed segment of the lens fibers (lamellae) is involved.

It seems to follow that all true idiokinetic defects of the lens are probably related to defects in germ plasm primarily, and identification of specific metabolic or enzymatic abnormalities in the near future is probably only a remote possibility.

Environmental Developmental Defects

In addition to the true developmental defects is a group of cataracts that are present at birth and arise mainly from maternal influences. The most important single cause of this type of congenital cataract has been shown to be rubella infection in the mother during the first three months of gestation. Gregg[27] in 1942 was the first to call attention to this association, which the reports of Swan,[28,29] Reese[30] and others[31-33]

firmly established as a clinical entity. The presence of associated congenital defects in most reports was striking and included especially congenital heart disease, deaf mutism and associated eye defects. In the large series of Swan et al.,[28] conducted under the auspices of the National Health and Research Council of Australia, a total of 49 mothers with rubella in the first trimester gave birth to 31 infants with congenital defects, 13 of whom had cataract. This early study suggested that congenital defects with a high rate of cataract formation followed in *all* infants when the rubella infection occurred during the first six to eight weeks of gestation, and in about 50 per cent if the infection occurred in the third month. However, the data recently presented by Ingalls and Purshottam[34] indicate that the true rate of congenital malformations after maternal rubella in the first trimester of pregnancy is probably no more than 17 per cent.

When cataracts in the infant follow maternal rubella they usually are readily seen and involve the lens extensively, requiring surgical measures for correction. Results have not been particularly good because of frequent associated eye defects. The proper approach to this entire problem necessarily involves such preventive measures as avoidance of contact with the infection during pregnancy, active immunization (exposure of young girls to the infection before pubertal change) and passive immunization with gamma globulin.

Other intrauterine infections implicated in this type of cataract include maternal syphilis, mumps, morbilli, varicella, influenza and toxoplasmosis. Cataracts occurring as a consequence of maternal syphilis are extremely rare but have been reported.[35] However, Friedenwald[36] does not include cataract in his very thorough report on the ocular lesions of fetal syphilis.

The occurrence of sporadic cases of cataract in the offspring of women who have had morbilli, mumps, influenza and varicella are mentioned by Sorsby,[7] and individual case reports of congenital cataract after maternal smallpox[37] and toxoplasmosis[38] have appeared. Snyder[39] was unable to detect any lenticular change in 74 infants of mothers who had been vaccinated during the first trimester of pregnancy.

Prematurity as an environmental factor in cataract formation has been mentioned by Bellows,[4] and in 2 cases reported by Guy[40] cataract developed that he ascribed to prematurity. Eames[41] was unable to correlate cataract formation with prematurity. In the past decade or so the more important problem of retrolental fibroplasia in premature infants has received considerable attention.[42] Studies by Ashton[43] and Patz[44] support the concept that high oxygen concentrations are harmful to the retina by inducing retinal arterial spasm, with resulting anoxia, and also that hypoxia per se is related to proliferation of retrolental fibroblasts. Although these concepts are accepted only in part by some investigators, notably Zacharias et al.,[45] it seems reasonable to accept the premise that reduced oxygen tension or vasospasm or both play more than a casual part in retrolental fibroplasia. The overgrowth of retrolental tissue often leads to secondary cataract formation, but usually this is only a part of the severe intraocular disorganization that results if progression of the primary disorder is not halted.

Congenital cataracts due to environmental developmental defects are thus seen to be largely limited to prenatal disease in the mother, the most important of which is rubella. Such conditions as prematurity and congenital syphilis are apparently quite unimportant in the genesis of this variety of congenital cataract.

Acquired Cataract

Most lenticular opacities appear after birth, and any cataract occurring in postnatal life up to the age of fifty is considered to be in this group.

Cataract Associated with Genetic Disorders

Common to this group of disorders are genetic abnormalities consisting of single or multiple inborn metabolic errors. Some of these specific defects have been identified in part, and others remain completely unexplained. The cataracts that are seen in these conditions are usually quite characteristic, and proper evaluation of the lens can aid materially in diagnosis.

Latent cataractous disorders. Sporadic reports of heredofamilial disorders associated with latent development of cataract have appeared.[46-52] Most of the patients have had associated congenital anomalies, but cataract as the sole defect has been described by Johnstone[46] and Cook.[50] Specific metabolic abnormalities were not identified in any of these cases, but certain anomalies, including mental retardation, ataxia and dental defects, appeared in several reports.[47-49,51] All cataracts developed within the first three decades of life, and, with the exception of those found by slit-lamp examination in several cases of epilepsy and unclassified mental deficiency,[51] the opacities were nuclear or lamellar in type, interfered with vision and required surgical intervention. The cases presented by Garland and Moorhouse[48] and Richards[49] seem to bear some resemblance to those recently reported by Lowe et al.,[53] in which bone disease, mental retardation, hypotonia, hyporeflexia and cataracts were described. The demonstration by these authors that their patients had specific absorptive defects of the renal tubules, including organic aciduria, suggests that defects in tubular function, with loss of essential nutrients (organic acids, amino acids, phosphorus and so forth), should be sought for in the latent cataractous states, especially in patients with multiple anomalies. It is certainly possible that loss of essential nutrients such as organic acids plays an important part in cataractogenesis, and it seems worth while to seek common denominators in many of

the heredofamilial disorders that are for the most part unclassified and neglected.

Mongolism. For many years since the original paper of Pearce, Rankine and Ormond[54] ophthalmologists have been familiar with lens opacities as a part of the syndrome of mongolism. The characteristic appearance of these cataracts has been described by Lowe[55,56] in a group of postpubertal patients with mongolism, and more recently Igersheimer[57,58] has adequately examined and described the lens change in 125 mongoloid idiots under slit-lamp visualization, many of the patients being prepubertal. The original paper by Pearce, Rankine and Ormond[54] reported lens changes as being present in practically 100 per cent of cases after the age of seventeen whereas the earliest changes did not occur before the age of eight. The appearance of lens opacities during puberty is confirmed by Igersheimer,[58] who failed to find any lenticular changes before the age of seven but stated that cataract became frequent after the age of ten and was almost always present after the age of sixteen. The significant cataracts are primarily flakelike and punctate opacities that are found mainly within the adult nucleus; they tend to progress very slowly, becoming somewhat more dense with time but not interfering to any significant degree with vision. Occasionally, with intense light, one can find "arcuate opacities" within the fetal nucleus that Lowe[55] considers quite characteristic of this disorder.

The identification of typical lens opacities can be useful in the differential diagnosis of mongolism from certain disorders that may resemble it. These include cretinism, nonmongoloid imbecility, epilepsy with deterioration, sequelae of birth trauma and many others.[58] The development of cataracts in the prepubertal period has led to much speculation regarding their possible pathogenesis, but to date no satisfactory explanation has been advanced. As in the other latent cataractous states continued research in mongolism regarding the pathogenesis of cataract seems necessary. The common occurrence of other abnormalities in mongolism, particularly dental abnormalities, led Spitzer and Mann[51] to suggest that the lenticular, dental and other ectodermal defects probably result from a common etiologic factor as yet unidentified.

Werner's and Rothmund's syndromes. In 1904 Werner[59] presented 4 cases of a heredofamilial disorder characterized by short stature, juvenile cataracts, marked premature aging and peculiar skin changes that were termed scleroderma. Rothmund,[60] in 1868, had described a family with cataracts occurring at a very early age, striking telangiectatic skin changes and some signs of premature senescence. "Werner's syndrome," as it is now referred to, was first reported in the American literature by Oppenheimer and Kugel,[61] who also reported the first autopsy findings in this country.[62]

It remained for Thannhauser[63] to define and classify Werner's and Rothmund's syndromes in relation to other genetically determined conditions associated with cataracts, premature aging and ectodermal dysplasias. Thannhauser concluded that both Rothmund's and Werner's syndromes were recessive hereditary disorders and that the observed abnormalities were due to multiple germ-plasm defects.

Cataracts were observed to be morphologically similar in both Rothmund's and Werner's syndrome, the main difference being their time of appearance; three months to three years in Rothmund's and twenty to thirty years in Werner's syndrome. The lens opacities were not particularly characteristic but were progressive, interfered with vision and required needling or removal. It was also pointed out that cataract was not encountered in the syndrome of progeria with nanism (Hutchinson–Gilford syndrome) or in that of hereditary ectodermal dysplasia (McKay–Davidson–Widderburn syndrome) — a useful aid in differential diagnosis. Cole et al.[64] presented 2 cases of ectodermal dysplasia with cataracts, but Thannhauser[65] refused to accept this, stating that the cases were in reality the first American-reported examples of Rothmund's syndrome and should be so considered, reaffirming his stand that cataracts are not seen in either childhood or adult life in hereditary ectodermal dysplasias. Moehlig,[22] in 1946, described a case of progeria in a child with congenital cataracts that Thannhauser was willing to accept. Approximately 59 cases of Werner's syndrome have now been reported in the literature,[67] many patients having the full-blown syndrome[66-69] and some presenting as the *forme fruste.*[70] No specific metabolic abnormality has been demonstrated to date in patients with Werner's syndrome even though several patients have been studied quite thoroughly.[69] It is curious that the cataracts are latent in this syndrome and that they often occur before other senescent changes are apparent, again suggesting some process that is going on before the disorder becomes obvious.

Myotonic dystrophy. Latent cataract is a constant feature of myotonic dystrophy. This heredofamilial disorder is characterized mainly by progressive muscle atrophy, with delay in relaxation of affected muscles, occurring primarily in the muscles of the face, neck and forearm. In addition, hypogonadism, loss of hair and dryness of the skin are fairly constant features of the syndrome. Batten and Gibb[71] were the first to establish myotonic dystrophy as a distinct clinical entity, and their original description of the disease has not been improved on to any great extent. Allen and Barer[72] adequately described the lenticular opacities, which they considered not only an early and constant finding but also quite characteristic in appearance. Early cataractous changes can only be seen with the slit lamp and consist mostly of small, dustlike subcapsular iridescent particles concentrated at the anterior and posterior polar regions of the lens. They are not stationary but progress to complete lens opaci-

fication, the rate often paralleling the speed at which muscular atrophy develops.[72] They are similar in appearance to the cataracts seen in mongolism and those occasionally encountered in hypocalcemic states. Waring, Ravin and Walker,[73] in their excellent clinical study, stated that the diagnosis of myotonic dystrophy could not be made on the basis of the lenticular changes alone but believed that a typical cataract found in a person with a family history of the disorder confirmed the presence of the disease regardless of the fact that no muscle dysfunction or associated abnormality was evident.

The cause of myotonic dystrophy is unknown. The disease is hereditary and shows the phenomenon of anticipation — that is, cataract and myotonia will appear earlier in each successive generation afflicted. The disease is most commonly observed to begin in the second or third decade and, as noted above, lenticular changes may be the earliest sign. Because hypogonadism is often a part of the syndrome, endocrine abnormalities have been looked for. Caughey and Brown,[74] in a study of 9 patients (7 males and 2 females), reported gonadal failure in 5 and myxedema in 2 cases, with uniformly low 17-ketosteroid excretion. There is little likelihood that these findings bear any direct relation to the pathogenesis of the disease since various forms of replacement therapy have not proved beneficial.[75] Furthermore, it has been shown that myotonia can be seen in primary myxedema, and if true myxedema is found in a patient with myotonic dystrophy, the addition of desiccated thyroid does not correct the myotonia.[76] Creatinuria is one of the features of myotonic dystrophy, but just when the creatinuria begins is unknown and its relation to the disease seems to be casual. The correlation in time of cataract development and muscular atrophy suggests that some common mechanism is involved. It is interesting that experimental cataracts produced by riboflavin and tryptophane deficiencies in rats are associated with gonadal failure, growth arrest and alopecia.[77] These experimental observations could have some bearing on the pathogenesis of this disorder.

(To be concluded)

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MEDICAL INTELLIGENCE

POLAROID PHOTOGRAPHY AS A PRACTICAL METHOD OF PROVIDING ILLUSTRATIONS OF RADIOGRAPHS FOR CLINICAL RECORDS

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ESSENTIAL for good medical practice is the maintenance of clear and concise medical records. That photographs of appropriate scale add immeasurably to the clarity and completeness of most clinical charts is simply to paraphrase the ancient adage, "One picture is worth a thousand words." This is particularly true of radiologic findings. Unillustrated verbal descriptions and interpretations, even when prepared by the most articulate radiologist, frequently leave too much to the imagination of the clinician. It is remarkable, in this golden age of graphic arts, that illustrative reproductions of significant radiographs are conspicuous chiefly by their absence in clinical records kept by most physicians. This omission has not been of the physician's making. In the past, conventional photographic methods have demanded too much skill, time, effort, equipment and space to lend themselves to routine use.

The need for a photographic process that combines simplicity and rapidity has been met by the development of a camera and film† by means of which dry prints of good quality can be produced in a few minutes. The compactness of this equipment makes it practical for any radiologist to provide the clinician with a suitably illustrated report of radiologic findings.‡ The method has additional advantages. Dry prints can be made and delivered to the clinician by the patient, long before the original films have been completely processed. The prints may be useful as an aid in discussions with the patient. As pointed out recently by Tager, quality is adequate for publication, when desired. The necessity for original films to pass out of control of the radiologist can be eliminated in most cases since small prints are usually better suited to the clinician's purposes.

The equipment required consists of an ordinary x-ray illuminator, the camera, close-up accessories, consisting of three lenses and a specially marked tape-measure, and a supply of the special type of film and paper. The ingenious design of the equipment is such that practically no photographic skill is necessary. A few minutes' study of the instructions supplied with each roll of film makes it simple for a veritable novice to prepare sharp, clear prints, measuring 7.2 by 9.7 cm., a convenient size for inclusion in record files. Of course, a little ingenuity and some knowledge of photographic methods can improve the speed and

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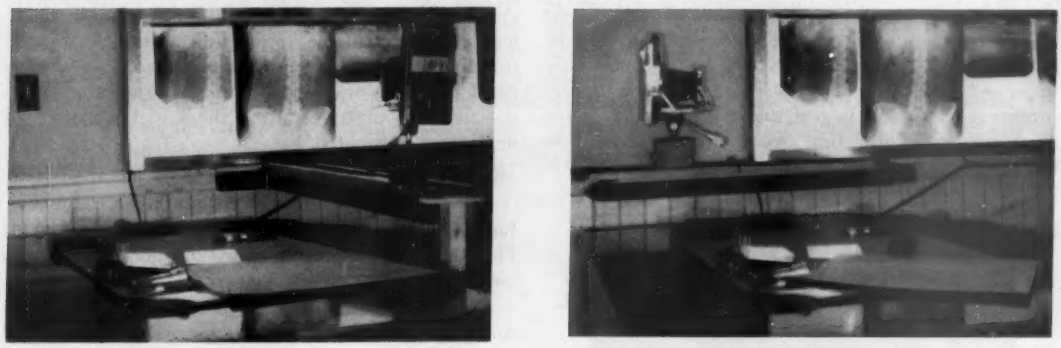
†Polaroid, available from the Polaroid Corporation, Cambridge, Massachusetts.

‡Tager, S. N. Use of Polaroid Land camera for copying roentgenograms. *Am. J. Roentgenol.* **71**:878-880, 1954.

simplicity of operation. Tager employs a copying stand, which is placed on a working counter, centered to an illuminator and moved to varying distances from it according to the size of the film to be copied; the distances for the various conventional film sizes are apparently marked on the surface of his counter. He does not mention any method of making his equipment available for immediate use without encumbering film-viewing space.

To have the equipment constantly at hand and yet out of the way during routine film viewing, I have devised a bracket that is attached by a strap hinge to the wall just beneath the illuminator regularly employed for film study. The hinge permits the entire assembly to be swung into position for immediate use (Fig. 1*A*) or to be placed to one side, but within easy reach, when not in use (Fig. 1*B*). The arm of the bracket includes a track along which the stand holding the camera may be moved for various distances from the film to be photographed. The points indicating the position of the camera for areas varying from 3 by 4 inches (7.6 by 10.2 cm.) to 17 by 22½ inches (43.2 by 57.2 cm.) are scored on the surface of the track. Some knowledge of rudimentary copying technics, such as cropping and dodging, makes it possible to improve the quality of original radiographs or to group significant areas from several radiographs in a single print.



A B

FIGURE 1. *Bracket Holding the Camera in Position for Use, with a Track for Varying Distance According to the Size of the Radiograph to be Photographed* (A), *and Swung Back into Position When Not in Use* (B).

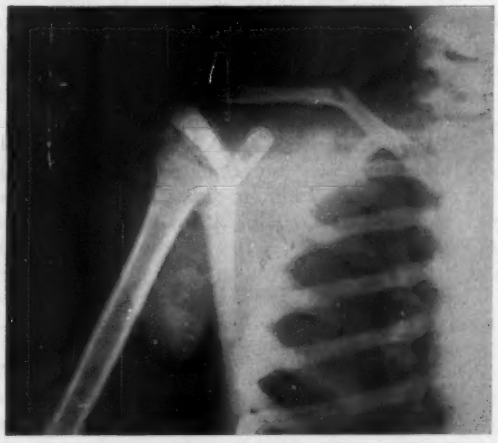


FIGURE 2. *Photograph (Actual Size) of a Radiograph Obtained from a Wet Film, Showing an Angulated Fracture of the Clavicle.*
The dry print was available to the clinician before the original radiograph was completely processed.

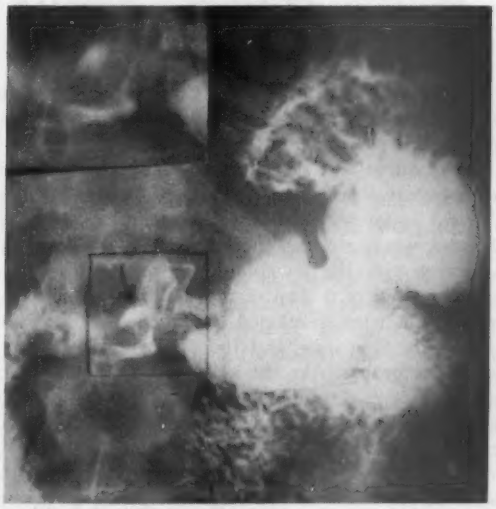


FIGURE 3. *Photograph of a Radiograph of the Stomach and Duodenum, with an Enlarged Inset Showing a Duodenal-Ulcer Crater.*

Figures 2 and 3 are reproductions, actual size, of prints made by this method for attachment to radiologic reports.

Summary and Conclusions

The use of a recently developed photographic process is proposed as a means of providing suitable illustrations for radiographic reports. It offers the following advantages: the completeness and clarity of physicians' clinical records can be immeasurably improved by illustrations of selected radiographs; the process is reasonable in cost, and the method requires no specific skill, little time, small effort and, because equipment is compact, minimum space; when delay is undesirable, dry prints can be made available to the clinician before the original films have been completely processed; by the use of illustrations the clinician can obtain better rapport with his patient; photographs of quality suitable for publication can be made immediately available from clinical records; by the substitution of satisfactory reproductions in diminished scale, loss of original films can be reduced, since the necessity of transmitting them to clinicians will be largely eliminated.

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CASE RECORDS
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Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 41151

Presentation of Case

A five-month-old male infant was admitted to the hospital because of a skin rash and an upper respiratory infection.

The patient was delivered normally at term after an uneventful pregnancy. Birth weight was 3.13 kg. He was apparently well until two months before admission, when a persistent skin rash, which initially appeared over the lower anterior part of the chest and consisted of a crop of macular red areas 1 to 3 mm. in diameter, developed. These lesions progressed to superficial scaling and then encrustation. There was some oozing from the scabbed sites, but no definite pus or vesicles. The lesions had gradually spread up to the neck and down to the abdomen and groin about three weeks before admission and to the scalp and arms as well as to the ears and mouth during the week before admission. On the extremities the lesions tended to appear first and most severely in the axillary creases, the elbows and the popliteal spaces. A white salve was used unsuccessfully for treatment of the skin lesions. No chemotherapy or other systemic medication had been administered. Three days before admission he began to have a nonproductive cough.

The dietary history was uneventful, and his appetite had been normal. He seemed to have gained weight. He was just beginning to sit up and hold his head up well at the time of admission.

Physical examination showed a 6.84-kg. infant with an extensive dermatosis, who appeared well developed and well nourished. Both external ear canals were filled with a weeping, crusted, confluent rash with several areas of excoriation. The drums were not visualized because of serous ooze from the canals. The orbital conjunctivas were slightly injected. The palpebral conjunctivas were erythematous, with several punctate, flat, dark-purplish-red lesions. The eyelids showed a dry, macular, finely scaly eruption over the medial angles of the upper lids. In the mouth there were purplish discolorations in several discrete sites along the alveolar margins. The scalp showed a moderately severe seborrhea. A prominent generalized, finely papular purpuric eruption was noted over the trunk and extremities (Fig. 1). In the axillary and neck folds there was also oozing and crusting. Multiple, round scales, 2 mm. in diameter, were scattered over the skin of the trunk. A few tiny vesicles were present. Fine papules, a few of which were excoriated, were present in the axillary, popliteal and antecubital spaces. Several vesicles as well as a maculopapular eruption were seen between the fingers. Papules were also visible in the palmar creases, where there was a striking hyperpigmentation. Axillary and inguinal lymph nodes were palpable, the largest measuring 1 to 1.5 cm. in diameter. The respiratory rate was rapid, with some subcostal retraction and no cyanosis. Breath sounds were coarse throughout, but no definite rales were heard. The heart appeared normal. A firm, smooth liver edge was felt 10 cm. below the right costal margin. The spleen, which was firm and smooth, was felt 6 cm. below the left costal margin. There was no edema or clubbing.

The temperature was 103°F., the pulse 160, and the respirations 50. The blood pressure was 120 systolic, 60 diastolic.

Urinalysis was negative. Examination of the blood revealed a hemoglobin of 10.6 gm. per 100 cc. and a white-cell count of 23,500 with 41 per cent neutrophils, 47 per cent large lymphocytes and 6 per cent atypical lymphocytes. Red cells and platelets appeared normal on the smear. The sodium was 135 milliequiv., the potassium 5.2 milliequiv. and the

chloride 94 milliequiv. per liter; the nonprotein nitrogen was 33 mg. per 100 cc. Old-tuberculin skin test was negative in a dilution of 1:1000. Stool cultures were negative for enteric pathogens. Throat culture gave a moderate growth of *Staphylococcus aureus*. X-ray films of the chest showed marked, ill defined increased densities throughout both lung fields (Fig. 2). Considerable emphysema of the lower lobes was noted. Films of the sinuses were normal, and there was very slight thickening of the right mastoid. X-ray films of both wrists showed the bone age to be approximately six months, according to Todd's standards. A skeletal survey disclosed no abnormalities.

On the second hospital day an operation was performed.

Differential Diagnosis

Dr. John M. Craig*: It appears to me that the symptomatology here falls into three fairly distinct categories: those of the skin lesions; those of difficulty with the lungs; and those of systemic lesions, with involvement of the spleen, liver and blood-forming organs.

The skin lesions started at about three months of age, appeared first on the trunk and tended to spread peripherally. In its initial form the rash was maculopapular, but it eventually became scaly and then oozing and crusted with ulceration. It was a persistent rash; it gave no evidence of clearing but continued to progress and spread peripherally. What skin lesions in children of this age must I consider? First, I think I may consider and dismiss fairly readily

Figure 1.

Ritter's disease or dermatitis exfoliativa neonatorum. The onset was somewhat late, and the lesions in Ritter's disease are not described as maculopapular; characteristically, in Ritter's disease, the skin desquamates in large sheets, leaving a raw area behind. The lesions may become secondarily infected, with resulting local and systemic effects. Leiner's disease or erythrodermia desquamativa, which is another possibility, has characteristic lesions quite out of keeping with those in the present case since by its title, erythrodermia, we should expect intensely red skin with frank scales. Moreover, there is an exudative diathesis in Leiner's disease, frequently an eosinophilia and a familial history of allergy. None of these were reported in this case. Impetigo can also be ruled out. This frequently starts on the face or buttocks and may spread rapidly, with the formation of vesicles, pustular areas and ulceration. Epidermolysis bullosa congenita usually begins at birth, starts on areas subjected to trauma such as the knees and elbows, and leaves raw areas behind, often with bullae both intraepidermal

Figure 2.

and occasionally subepidermal. There is no evidence that a blood Hinton test for syphilis was obtained on this patient. However, one would expect the skin lesions of syphilis to have been present at birth, less maculopapular, and more brawny, with desquamation, and primarily to have involved the mouth or anus; none of these were found here. Infantile eczema is more difficult to rule out. The time of onset is not uncharacteristic, although the point of onset, over the trunk, is less in keeping with eczema, which usually involves first the face and the scalp and later the popliteal and antecubital spaces.

I think I must also consider generalized moniliasis of the skin. I suspect that if the child's skin had been cultured, monilia or candida organisms certainly would have been found, since these organisms can frequently be cultured from an already damaged skin. There was no evidence of thrush, severe debility or exposure to long-continued antibiotics, which may lead to such a state.

*Associate pathologist, Children's Medical Center; associate in pathology, Harvard Medical School.

Finally, I must consider Letterer–Siwe disease or nonlipid histiocytosis or reticuloendotheliosis. The lesion, I believe, fits very closely with this condition — a maculopapular lesion, infiltration in the skin probably being the primary lesion, followed by crusting, oozing and ulceration. The lesion often first appears on the trunk although careful questioning of the mother, I understand, may reveal that the first lesions were on the scalp. The spread from the trunk to the periphery, the involvement of the mucous membranes, conjunctiva and especially the external and middle ears are quite consistent with Letterer–Siwe disease.

Next I shall consider the pulmonary lesions. The fundamental symptomatology and findings appear to have been a nonproductive cough; some respiratory obstruction, without evidence of obstruction of the trachea or laryngeal level; and a rapid respiration, with perhaps carbon dioxide retention as evidenced by the low serum chloride (although the sodium was not elevated as one might have expected). There were no localizing signs by auscultation, and lastly, in the x-ray examination, fine markedly increased densities with evidence of emphysema were noted. May we see the x-ray films?

Dr. C. C. Wang: Examination of the chest done on admission shows diffuse pulmonary change in both lung fields consisting of fine infiltrations and considerable emphysema of the lung bases. The diaphragm lies fairly low and is flattened; the heart is not unusual. On the film of the chest one can see that the spleen and liver are markedly enlarged. The films of the chest taken approximately a month later show no significant change. Survey films of the long bones demonstrate no bone destruction.

Dr. Craig: What conditions must I consider in view of the lung findings? Aspiration pneumonia in children of this age certainly always impresses the pathologist. The distribution — more disease in the upper lobe than the lower — is not inconsistent with aspiration pneumonia although the fine pattern of the process is somewhat against it. Nothing in the history or physical findings suggests the leading causes for aspiration pneumonia — namely, central-nervous-system disease, severe debility or a tracheoesophageal fistula, associated with a feeding difficulty.

Tuberculosis is a possibility although the lack of progression of the lesions is certainly not in keeping with it, and the negative tuberculin test tends to rule it out. There was not a family history of tuberculosis, which is important in children under two years of age, although a child at the Children's Hospital who died of miliary tuberculosis had a negative family history and was only out of the hospital for four days of his four months of life. In the case under discussion the liver and spleen were certainly larger than one would expect with tuberculosis. The skin lesions are very difficult to fit in with this diagnosis.

With these lung lesions generalized moniliasis, I think, must again be considered. We have seen children of this age with diffuse, generalized moniliasis of the lungs and other parts of the body. There was no evidence of thrush or of the long-continued use of antibiotics, or ACTH or cortisone therapy, all of which appear to be related to the spread of generalized moniliasis.

I think syphilis can be easily eliminated.

Generalized mucoviscidosis is a possibility although the lesions were much finer than those usually seen in that disease. There were no other signs of pancreatic fibrosis such as poor nourishment, foul stools or a productive cough.

I think I can also eliminate two other processes: congenital agammaglobulinemia, largely on the basis of the tremendous size of the spleen and lymph nodes, and hypergammaglobulinemia, on the basis of the general good nutrition of the child.

Of the storage diseases, Niemann–Pick disease may give such infiltration in the lungs as this child had. However, a family history was lacking, and this child apparently was not of Jewish parentage, which is also of importance although not absolutely necessary in the diagnosis of Niemann–Pick disease. Finally there was no evidence of central-nervous-system degeneration, a common feature of Niemann–Pick disease.

Letterer–Siwe disease, again, must be considered seriously. The type of infiltration is consistent with the disease, as is its persistence. The emphysema is also consistent. The infiltration of Letterer–Siwe cells into the terminal bronchioles may give rise to emphysema and even cystic formation in the lung.

Finally, in discussing the general visceral involvement, I can eliminate the heart, kidneys and pancreas and turn my attention to the liver, spleen, lymph nodes and blood. An anemia was present. It would be helpful to know whether there were reticulocytes in the peripheral blood — that is, whether there was evidence of increased destruction of red cells or simply depression of their production. I know that there was an elevated leukocyte count, with abnormal forms, presumably lymphocytes, that the skeletal films were normal and that the child had a fever. Primary liver disease I think I can eliminate by the absence of jaundice and bile in the urine. It would be helpful to know what the flocculation tests were, because Letterer–Siwe disease is one of the more common causes of positive flocculation tests in this age group. There was no good evidence for fatty infiltration of the liver. The enlargement of the liver I must ascribe, then, to cellular infiltration into it as well as into the spleen.

What other infiltrative processes must I consider? Leukemia is one and can probably only be eliminated by biopsy of bone marrow or lymph nodes. Moreover, except in eosinophilic leukemia, it is unusual to find a diffuse infiltration of lung, and as far as I know those infiltrations do not cause symptoms. I think the same objections may be raised to lymphoma, in which the lung lesions are much more likely to spread diffusely from the hilus than to be fine, punctate diffuse lesions throughout the lungs.

Of the storage diseases, Gaucher's disease must be considered. With Gaucher's disease at this age the child would certainly have had central-nervous-system symptoms and bone lesions, neither of which was present. Also, with Niemann–Pick disease, there is degeneration of the central nervous system. In this child, moreover, the eye signs of Niemann–Pick disease were lacking; often, there is a cherry-red spot in the macula.

Again, I come back to Letterer–Siwe disease, with the large liver and spleen. Anemia is not uncommon; this may result partly from bleeding, partly from erythrophagocytosis, which has been noted by the hematologist, and partly from infiltration and replacement of the bone marrow. The purpuric skin lesions, which were present late in the course, may or may not be associated with a low platelet count. I believe that this patient had Letterer–Siwe disease and suggest that the biopsy showed infiltration of the skin and of the lymph nodes. If a bone-marrow biopsy was also obtained, it may or may not have shown lesions within the marrow. We have had, in a recent week, one case in which a biopsy of the sternal bone marrow gave no evidence of Letterer–Siwe disease but a biopsy of the tibia, uninvolved by x-ray examination, showed florid infiltration with Letterer–Siwe cells.

DR. BENJAMIN CASTLEMAN: Dr. Lever, have you any comment about the skin lesions?

DR. WALTER F. LEVER: I think that the skin lesions are characteristic of reticuloendotheliosis — the scaling and crusted papules, the purpuric component and the distribution, including involvement of the auditory canals, the mucous membranes of the mouth and the conjunctivas, as has frequently been pointed out. The eruption resembles seborrheic dermatitis in its scaling and its distribution over the scalp and the center of the trunk, but it differs from it by the presence of distinct papules and of petechiae.

DR. CASTLEMAN: Dr. Wang, what do you think about the lesions in the lung?

DR. WANG: I think these changes in the lungs and the enlargement of the spleen and liver are consistent with Letterer–Siwe disease.

CLINICAL DIAGNOSIS

Letterer–Siwe disease.

DR. JOHN M. CRAIG'S DIAGNOSIS

Letterer–Siwe disease.

ANATOMICAL DIAGNOSIS

Letterer–Siwe disease.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The operation was a biopsy of the skin, which confirmed Dr. Craig's diagnosis of Letterer–Siwe disease (Fig. 3). The patient gradually failed, and ascites developed; he died about a month later. At autopsy we found approximately 400 cc. of ascitic fluid, probably because the serosa of the entire gastrointestinal tract was thickened and on microscopical examination showed infiltration with histiocytes quite characteristic of Letterer–Siwe disease. We found a fair amount of infiltration in the spleen,

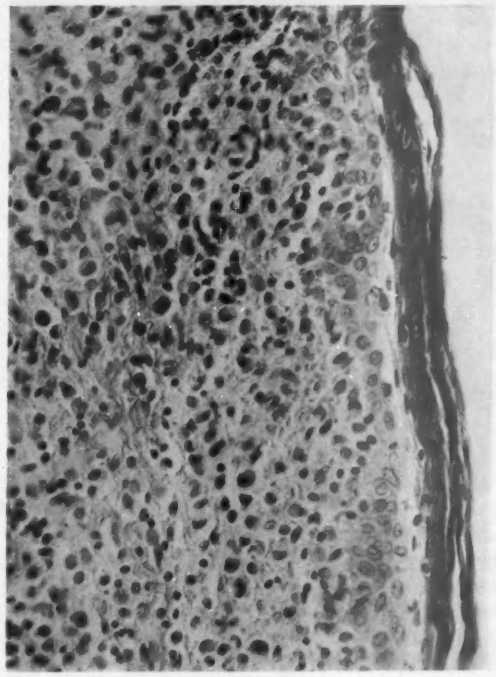

FIGURE 3.

which was three times the normal weight. The liver was about twice the normal size and also was infiltrated with histiocytes. The kidneys were very pale but were not increased in size. I believe the pallor was due to the anemia, for there was no infiltration of histiocytes in the kidneys.

The lungs, which were the highlight of the autopsy, showed marked infiltration (Fig. 4), which was obvious on gross inspection. There were nodules surrounded by a compensatory dilatation of alveoli that eventually led to emphysema, as was seen in the x-ray films.

The lymph nodes, especially the mesenteric and retroperitoneal lymph nodes, were extensively involved. The histiocytes had replaced the nodes, leaving only a few lymphocytes scattered here and there.

Dr. Craig, should you like to comment upon the relation of this disease to eosinophilic granuloma and Hand–Schüller–Christian disease?

DR. CRAIG: It is believed that, pathologically, at least, there is a continuous spectrum of histologic variants from Letterer–Siwe disease on the one hand to eosinophilic granuloma on the other. The very young children have Letterer–Siwe disease. One can

hardly get away from the idea that this is actually a malignant proliferative process in some cases, for we have seen several cases in which large numbers of cells of this type appeared in the peripheral blood, with massive infiltrations on the pericardium and other areas of the body. So at one extreme of the spectrum

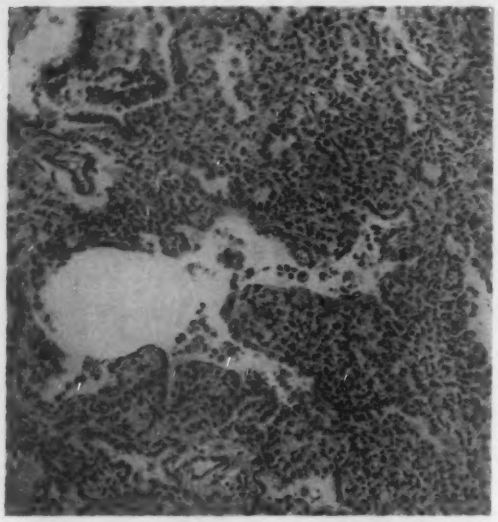

FIGURE 4.

there is this almost tumorous process. Then at another point in the spectrum in the slightly older children the infiltration is less marked and after a time often shows some lipidization or an increased amount of cholesterol and lipids within the cells. In the older age group, the process is also much less likely to be diffuse, but is more localized. The patients with fatal visceral involvement have an age at onset of less than a year. If the visceral involvement is nonfatal, the age at onset is somewhat later— a little over a year. In those with multiple bone involvement, the age at onset is three years or more. When there are one or two bone lesions of eosinophilic granuloma, the age at onset is still later, and, finally, when there are single bone lesions — the point in the spectrum of isolated eosinophilic granuloma — the age at onset may be around eight or nine years. At the eosinophilic-granuloma end of the spectrum the pathologic process is similar to that seen in Hand–Schüller–Christian syndrome.

DR. H. L. HEYL: Is this only a child's disease?

DR. CRAIG: It is always difficult to exclude on histologic grounds alone. I emphasized histologic and pathological grounds because we do not know the etiology of any of these conditions — whether they are infections, neoplastic or metabolic. We may be talking about groups of different diseases with no etiologic relation to one another. Cases in adults have been reported. There has been 1 recently at the City Hospital. If one looked at the skin alone in that patient it would be impossible to exclude Letterer–Siwe disease, although the man was nearly sixty years old.

DR. CASTLEMAN: There have been cases in adults. One that I know showed a pulmonary picture exactly like this.[1] That was the reason why Lichtenstein[2] prefers to call this whole series of cases Histiocytosis X. He would rather call it that to show that we know very little about it and that perhaps more work should be done to find the etiologic agent. He believes that they are all in the same family. Cases are being reported, sporadically, with exactly the same picture in adults as are seen in children.

DR. HEYL: But one gets the impression that there are many more children with these rare conditions.

DR. CASTLEMAN: There is no question about that, — they are mostly in children, — but the fact that an occasional case bridges the gap between Letterer–Siwe disease, Hand–Schüller–Christian disease and eosinophilic granuloma makes one speculate that perhaps the etiologic agent may be the same.

DR. DEAN L. MOYER: How are these cases being treated at the Children's Medical Center?

DR. CRAIG: Now they are being treated by the tumor-therapy group with ACTH, which seems to be the most effective. Cortisone may be effective in some cases. We have also used nitrogen mustard with much less effect and the antifolic drugs — Amethopterin and that group — perhaps with the least effect. In the florid cases, in which the onset is at a very young age, with purpuric rash, splenomegaly and lymphadenopathy, the physicians have been able to increase the duration of life about seven or eight months, but that is all. The older children have a much better prognosis. The child under discussion here had four of the features that probably give the worst prognosis for survival — very early onset, purpuric rash, hepatosplenomegaly and lymphadenopathy. The children in the older age group, whose disease starts at the age of two or so, may survive for years and may eventually go on to healing. We know from their natural history that that occurs; how much therapy has aided those in that age group is difficult to tell.

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CASE 41152

PRESENTATION OF CASE

A sixty-four-year-old refrigerator-maintenance man was admitted to the hospital because of convulsions.

The history was obtained primarily from the patient's wife, who said that he had apparently been well and working until a month previously, when he complained of diplopia for a few days. Two weeks later he began having generalized severe headaches,

which improved after a few days. Irritability was also noticed at this time. Twelve days before admission, while he was driving his car, his wife noted that during a conversation he became confused, although he was able to drive home. His physician found no abnormality. As the physician was about to leave, however, the patient gave a groan, stiffened out with arms extended, and had bilateral clonic movements that were greater on the right side. There was no incontinence. Weakness on the right side and difficulty in speaking were present for several hours after this convulsion. He was then admitted to another hospital for a period of five days. A lumbar puncture yielded cerebrospinal fluid that contained 14 red cells per cubic millimeter and a protein of 62 mg. per 100 cc. He apparently recovered completely from this episode and was relatively well during the hospital stay. He remained well for the following week, but his wife observed that when he drove his automobile his responses to traffic conditions were slow and that his gait seemed unsteady. On the day before admission he became awkward in using the right hand, and was drowsy. Headache was again prominent. On the evening before admission he suddenly had a "surprised" look, stared and slumped to the floor. A convulsive seizure occurred, predominantly affecting the right side. He remained unconscious for several hours, but later was up and active again, although he was confused. He was brought to the hospital shortly afterward.

The past and family histories were noncontributory except for a high blood pressure for several years.

Physical examination revealed a confused, obese, plethoric man in no apparent distress. There was no stiffness of the neck. A small laceration was present on the left side of the tongue.

Examination of the chest showed an increased anteroposterior diameter, with many coarse rhonchi and increased resonance. The heart was enlarged, the left border extending to the anterior axillary line, with a basal Grade 2 systolic murmur. The aortic second sound was greater than the pulmonic. Carotid pulsations were normal. The abdomen was not remarkable.

On neurologic examination the patient was disoriented in time and place. He was lethargic, but tried to co-operate. He was unable to read, to name familiar objects well or to perform simple calculations, and he followed simple commands poorly. Perseveration was marked. Vision was difficult to test, but seemed impaired although he was able to count fingers and grasp objects held in front of him. The visual fields were considered full. The optic-disk margins were questionably blurred; the retinal arterioles were narrowed, and there were a few small "exudates." He could not open his eyes completely. There was slight impairment of abduction of both eyes, and a few nystagmoid jerks were noted on lateral gaze. Convergence was poor. Upward gaze did not appear to be full in range. The pupils were of normal size and reacted briskly to light. The patient was right-handed. Strength was not thought to be impaired, although there had been a question of slight weakness of the right-hand grip when he was first seen. There was increased resistance to passive motion in all four limbs. Gait appeared normal, except for unsteadiness on attempted heel-to-toe walking. There was no specific ataxia of the limbs. Tendon reflexes were brisk, and were somewhat more active on the right. There was sustained ankle clonus on the right and none on the left. Abdominal reflexes were absent, and cremasteric reflexes present and symmetrical. The right plantar reflex was equivocal; the left was extensor. Positive Oppenheim, Chaddock and Gordon signs were also present on the left. Sensory examination was thought to be negative.

The temperature was 98°F., the pulse 72, and the respirations 20. The blood pressure was 190 systolic, 120 diastolic, in the right arm and 180 systolic, 110 diastolic, in the left.

Urinalysis was negative. Examination of the blood revealed a hemoglobin of 15 gm. per 100 cc. and a white-cell count of 12,500, with a normal differential. The nonprotein nitrogen was 38 mg. per 100 cc., and the sodium 133 milliequiv., the potassium 4 milliequiv., the carbon dioxide 28 milliequiv., and the chloride 90 milliequiv. per liter. The prothrombin time was 15 seconds (normal, 13 seconds). On lumbar puncture the initial spinal-fluid pressure was equivalent to 240 mm. of water, with a final pressure of 140 mm. after removal of 6 or 7 cc. of fluid. The fluid was clear, but slightly xanthochromic, gave a ++ Pandy test and contained 20 red cells and 55 white cells per cubic millimeter, of which 49 were lymphocytes. The protein was 200 mg., and the sugar 92 mg. per 100 cc. Culture was negative for bacteria. A stool guaiac test was negative. An electroencephalogram was diffusely abnormal, with irregular 2- to-4-per-second slow waves up to 100 microvolts bilaterally. There were no phase reversals or other focal signs. The slow activity was a little more prominent on the left. An electrocardiogram showed a normal sinus rhythm, with widespread nonspecific ST-segment and T-wave changes consistent with myocardial ischemia. Roentgenograms of the skull revealed prominent vascular markings in the right parietal region. The pineal gland was calcified but not displaced. There was a large calcification in the anterior portion of the falx. A slight degree of calcification was also noted in the left choroid plexus. X-ray films of the chest showed enlargement of the left ventricle and a tortuous aorta.

Subsequent examinations confirmed the presence of spasticity in all four extremities, with bilateral Babinski signs and ankle clonus on the right. Lethargy was striking. By the third hospital day both disk margins were considered to be blurred. The patient ignored pinpricks in the right arm and hand when both sides were simultaneously stimulated. More complete sen-

sory testing was not possible. The right leg on one occasion moved less well than the left, although this was not consistent. Tendon reflexes became slightly more active on the left. Abdominal reflexes were active bilaterally. Ankle clonus was present on the left. Bilateral Babinski signs persisted.

The patient's general condition declined steadily, chiefly his state of consciousness. He remained afebrile. On the third hospital day, bilateral occipital burr holes were made; there were no remarkable findings except for marked dilatation of the cortical veins on the left. On the next day a ventriculogram revealed an initial pressure equivalent to 300 mm. of water in the right lateral ventricle; 10 cc. of air was introduced, and subsequently another 15 cc. The films revealed a symmetrical pressure defect involving the superior surfaces of the lateral ventricles, producing sharp, pointed superolateral corners of the bodies of the ventricles (Fig. 1). The septum pellucidum was not thickened. The third ventricle was seen very poorly. No shift of midline structures was noted, and the ventricles were not dilated. Examination of the cerebrospinal fluid taken at the time of the ventriculogram revealed 4 red cells and 1 white cell per cubic millimeter. The protein was 160 mg. per 100 cc., and the colloidal-gold test 1111232211. On the next day the patient was slightly more alert, but was unable to speak. He moved all four limbs, but the left more than the right. Two days later a pneumoencephalogram confirmed the previous findings and demonstrated normal third and fourth ventricles. On the same day a trephine craniotomy was performed, with a biopsy of the region of the corpus callosum.

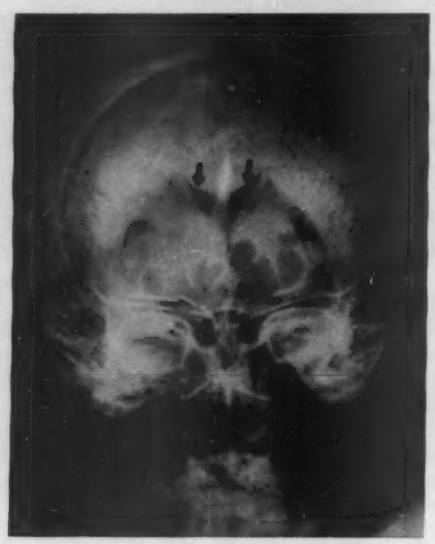

FIGURE 1. *Posteroanterior View of the Skull after Air Filling of the Ventricles.*
Arrows indicate unusual compression of the roofs of the lateral ventricles.

The brain was noted to be markedly swollen. Pathological examination of the tissue removed at biopsy did not reveal tumor.

Postoperatively, the patient was totally unresponsive, but vital signs were well maintained. The pupils were equal, but sluggishly reactive. By the following day his condition had worsened slightly. Regular respirations gave way to a gentle waxing and waning of breathing, without periods of apnea. Pupils remained equal. He remained in coma with eyes fixed in midline gaze. During the afternoon of the second postoperative day, he vomited 500 cc. of brownish fluid. About an hour later there was a sudden deterioration in vital signs, with a blood pressure of 60 systolic, 40 diastolic, and gasping respirations. He died three minutes later.

DIFFERENTIAL DIAGNOSIS

DR. MAURICE VICTOR*: We might suitably retrace the history to see what can be made out of some of the individual symptoms and signs. The first symptom was diplopia of a month's duration. An unqualified statement of this sort, which does not tell us whether the patient truly had double vision or simply blurring of vision and whether or not it persisted, does not give us much help; I shall have to put it aside for the moment. The important symptomatology seems to have begun two weeks before admission, with severe generalized headaches, followed a few days later by confusion and a major seizure, more prominent on the right side, weakness of the right side and difficulty in speaking. This post-ictal weakness and aphasia probably represented a Todd paralysis, and is strong evidence for a focal lesion in the left cerebral hemisphere. Even at this time, the spinal fluid revealed an abnormal protein content, 62 mg. per 100 cc. The patient did not make a complete recovery; his mental activity remained slow and his gait unsteady, and he had another seizure, again more prominent on the right side.

Presented with such a history, which is essentially one of focal seizures beginning at the age of sixty-four, one would immediately suspect a serious neurologic disease. And we might suitably mention the disorders that ordinarily cause seizures for the first time at this age: alcoholism, trauma, neurosyphilis, vascular lesions of the brain and neoplasm. I think that the history adequately rules out trauma and alcoholism. Furthermore, alcoholism per se is not a cause of focal seizures; therefore, whenever alcoholism and focal seizures are both present some focal cause apart from the alcoholism must be sought to explain the seizures. Neurosyphilis will be mentioned later. On the basis of the history alone one would consider neoplasm and vascular disease as the two major possible diagnoses.

He was disoriented and lethargic, was unable to read, to name familiar objects, or to perform simple

*Assistant neurologist, Massachusetts General Hospital.

calculations and followed simple commands poorly. These signs indicate more than simply a generalized depression of brain function and resultant confusion. I should interpret them as representing an aphasic disorder, and when they are coupled with the speech disturbance and the right-sided paralysis that followed there is little doubt that we are dealing with a focal lesion of the left cerebral hemisphere, most probably of the parietal or temporoparietal region. We are told later on that the patient was right-handed. The ocular signs listed in the protocol do not help us in localizing the disease process. The incomplete opening of the eyes, the slight impairment of abduction of both eyes, the few nystagmoid jerks, the poor convergence and the fact that upward gaze did not appear to be full in range could all be attributed to the patient's age or to his general state of depression of consciousness; perhaps the inability to abduct both eyes fully was due to increased intracranial pressure, the sixth nerve being affected. However, there is not enough evidence that the brain stem was the seat of focal neurologic disease.

The increased resistance to passive motion in all four limbs, a sustained ankle clonus on the right and none on the left, and a plantar reflex equivocal on the right and extensor on the left are evidence of a lesion or lesions in the right cerebral hemisphere as well as the left. The interruption of corticospinal-tract projections was most probably at the cerebral level since there was no clear indication of brain-stem disease.

The findings on lumbar puncture present a difficult problem. If this man was fully relaxed when the puncture was done, a cerebrospinal-fluid pressure equivalent to 240 mm. of water must be regarded as definitely increased. How should I regard the xanthochromic fluid? This is difficult for me to decide, since an elevated protein of this degree is in itself capable of producing faint xanthochromia; actual hemorrhage, therefore, need not be implicated as the cause of the xanthochromia. The finding that bothers me most is the 55 white cells in the cerebrospinal fluid, 49 of which were lymphocytes. I do not know whether I am justified in assuming that the other 6 were polymorphonuclear leukocytes or not. Does anyone know?

Dr. Edward P. Richardson, Jr.: I believe they were polymorphonuclear leukocytes.

Dr. Victor: A spinal-fluid pleocytosis such as this raises the question of cerebral abscess. There was no obvious source for abscess, such as infection in the lung, sinuses or middle ears, and the patient was afebrile throughout the illness. Isolated cases of brain abscess do occur in the absence of fever and an obvious source of infection. If one were to postulate cerebral suppuration, it would have to take the form of multiple abscesses. This is a rare pathologic state, seen in conjunction with severe septicemia and other signs of severe generalized infection; we can therefore dismiss it.

On the basis of the spinal-fluid findings one should also think of focal embolic encephalomalacia, the result of subacute bacterial endocarditis, but again we have no evidence for such a diagnosis.

For obvious reasons we can also exclude viral illnesses or, for that matter, tuberculous meningitis. Syphilitic meningitis has to be considered, and I shall say a word about that later.

The electroencephalogram was diffusely abnormal and simply tells us what we already know from physical examination: that the patient had a diffuse disturbance of the brain, a little more severe on the right than on the left. The electrocardiogram does not help much. There was a myocardial ischemia, but no clear-cut evidence of a myocardial infarct that might have been the source of emboli to the brain. Both disk margins became blurred in the course of the illness — additional evidence of increased intracranial pressure. The patient ignored pinpricks in the right arm and hand when both sides were simultaneously stimulated. Apparently, he was able to perceive each stimulus separately. This phenomenon, for practical purposes, may be regarded as a sign of parietal-lobe disease and would confirm our suspicion that he was harboring a crude lesion or lesions in the left temporoparietal region.

On the third hospital day, quite correctly I think, burr holes were made in the skull. The dilatation of the cortical veins on the left probably has some meaning, but unfortunately I do not know what it is; the important thing, however, is that a subdural hematoma was not found.

The next important point was the air study; I think we might look at those films.

Dr. John F. Gibbons: The chest film shows the heart to be enlarged, particularly in the region of the left ventricle. There is widening and dilatation of the aorta. There is no significant abnormality in the lungs. The other films are those of the skull and those taken incidental to the ventriculogram and encephalogram. The ventricular system is midline on all sagittal views. There is no shift and no particular dilatation of the ventricles. The protocol mentioned the configuration of the superior surfaces of the lateral ventricles, which can be seen (Fig. 1) on the anteroposterior view, in which the anterior portions of the lateral ventricles are partially filled. On the posteroanterior view the posterior portions of the lateral ventricles are filled. There is an unusual deep indentation of the part of the ventricular roofs that represents the area of the corpus callosum. The various other films from both air studies fail to reveal any localized lesion or dilatation or disfigurement of the ventricular system. The temporal horns are not ideally filled on the studies so the temporal horn on one side or the other may be minimally affected, but I cannot be sure of it from the films. The calcifications mentioned in the protocol are physiologic ones — namely, in the falx anteriorly and in the choroid plexuses bilaterally. The pineal gland is calcified and is not displaced. There is no evidence of bone erosion. The pituitary

fossa is normal. To summarize, the only significant finding is the change that may indicate thickening or at least unusual prominence of the corpus callosum.

DR. VICTOR: Obviously, the Neurological Service thought in exactly the same way because on the basis of this finding a trephine craniotomy was done anteriorly and a portion of the corpus callosum was removed for examination.

Certainly, one's first inclination is to make a diagnosis of neoplasm. One would have to consider secondary neoplasm, since we have to account for multiple lesions in the brain. There was nothing in the history or the physical examination to involve the lungs, the kidneys, the gastrointestinal tract or the thyroid gland, which are the common sources of secondary brain tumor. Nor was there any reason to suspect a melanoma or any of the rarer types of tumor that metastasize to brain.

Could this have been a primary tumor of the brain — a glioma of the corpus callosum? Certainly, the entire history is compatible with such a diagnosis, and the air studies very suggestive of it. The clinical and spinal-fluid patterns, however, although compatible with a glioma of the corpus callosum, are not absolutely classic. The course of the illness was measured in weeks. That is a short course even for a glioma of the corpus callosum. The clinical syndrome that is most characteristic of a tumor of the corpus callosum is one of progressive dementia with a normal spinal-fluid pressure until late in the disease. In a report of 20 cases of glioma of the corpus callosum verified at autopsy, Schlesinger[1] found an elevated spinal-fluid protein in only 4. Obviously, these are weak arguments. Although it would be unusual a glioma of the brain could evolve in this rapid manner and give rise to 49 lymphocytes and a protein of 200 mg. per 100 cc. in the spinal fluid. I think that the strongest argument against the diagnosis of tumor, however, is the pathologist's report that no tumor tissue was seen in the biopsied specimen. One might simply disregard this report and assume that the biopsy was taken from an area in which there was no tumor. But, certainly, if any area was likely to yield tumor, this was it. It would be my inclination, therefore, to accept the biopsy report. I assume that it would be unfair to ask what it did show; the positive findings were not mentioned, probably because they would have revealed the diagnosis.

If the possibility of tumor is put aside, the only diagnosis that one need seriously consider is vascular disease of the brain. Almost surely, though, this clinical picture was not the result of the common vascular accidents that affect the brain. This was not the usual story of spontaneous cerebral hemorrhage or embolic and thrombotic occlusive disease. There was no obvious source of emboli and no evidence of emboli to other parts of the body. The spinal-fluid protein was entirely out of line with that usually seen in embolic and thrombotic occlusion of the vessels. One must cast around, then, for the more unusual types of vascular disease of the brain. One of these is meningovascular syphilis. Nowhere in the protocol is there any mention of the serologic reactions of the blood or spinal fluid. I assume that they were negative. Is that a proper assumption?

DR. RICHARDSON: There is unfortunately no report to indicate that these tests were done.

DR. VICTOR: We must rely, then, on clinical criteria alone. The tempo of this illness was far more rapid, and the entire aspect of the disease was more fulminant than what is seen in meningovascular syphilis or general paresis.

Another type of vascular disease that should be mentioned is cortical venous thrombophlebitis or thrombosis. Cortical thrombophlebitis occurs most often as a complication of suppurative disease of the brain, meninges, middle ear or sinuses. Bland thromboses tend to occur in the post-partum or postoperative period, or in marantic children. This was not the setting for cortical thrombophlebitis or thrombosis. Furthermore, on craniotomy, the veins were reportedly dilated, but not thrombosed; we can therefore dispense with this diagnosis.

There remain to be considered the inflammatory diseases of cerebral vessels. This class of diseases is frequently neglected in the differential diagnosis of cerebrovascular disorders. The pathologic states included comprise Buerger's disease of the cerebral vessels, giant-cell arteritis, polyarteritis nodosa and granulomatous angiitis. Buerger's disease of the cerebral arteries is a rare disorder, affecting young adults and usually the larger vessels, such as the carotid artery; it can safely be excluded in the patient under discussion. In temporal or giant-cell arteritis, there is usually visible evidence of arterial disease, either over the scalp or in the eyegrounds, as well as localized headache, fever and leukocytosis. Rare forms of polyarteritis nodosa may affect the central nervous system; pathologically, they take the form of an infectious granulomatous arteritis. Such an illness may be accompanied by asthma and eosinophilia, but this is not necessarily so. A few months ago a patient was presented at neurologic grand rounds, and his illness had much the same tempo as that of the patient under discussion. A biopsy of his cerebellum showed a granulomatous angiitis. Meyer et al.[2] have described a case of granulomatous angiitis whose clinical course was practically identical with this patient's. It is in this class of illness that I think our patient's disease belongs, and I shall put it forth as the diagnosis, though without much confidence, with a glioma of the corpus callosum as a second choice.

CLINICAL DIAGNOSIS

Glioma of the corpus callosum.

DR. MAURICE VICTOR'S DIAGNOSIS

Granulomatous angiitis of the cerebral arteries.

Anatomical Diagnoses

Granulomatous and necrotizing arteritis of cerebral arteries.
(?Polyarteritis nodosa.)
Cardiac hypertrophy, hypertensive type.
Pulmonary edema and infarction.
Bronchopneumonia.
Nephrosclerosis.

Pathological Discussion

Dr. Edgar B. Taft: At autopsy this patient was well developed and well nourished, but according to the prosector, was not particularly obese. The heart was greatly enlarged, weighing 670 gm. There was a mild coronary sclerosis, and microscopical examination showed a small amount of myocardial fibrosis, which was not particularly prominent but was diffuse. There was severe atherosclerosis of the aorta but no evidence of syphilitic involvement. There was a small fusiform arteriosclerotic aneurysm of the right common iliac artery. The lungs were very heavy — together they weighed 1550 gm. — and were congested and edematous. On microscopical examination there were small foci of pneumonia, which was thought to be terminal. The kidneys, surprisingly, weighed together 300 gm., approximately the normal size, and grossly were not thought to be abnormal. Microscopically, however, there was severe vascular disease of the arteriosclerotic type such as we see in patients with hypertension. Even though this patient had a nonprotein nitrogen of only 38 mg. per 100 cc. we believe that almost certainly, if he had not died of the brain disease, he would have gone into renal failure before much longer. The most important part of the autopsy is in Dr. Richardson's field.

Dr. Richardson: The brain appeared very much swollen, with marked flattening of the convolutions, and was extremely heavy, weighing 1750 gm. The large arteries showed severe atherosclerosis. There was pronounced grooving of the medial aspects of the temporal lobes bilaterally, indicating a severe degree of herniation through the tentorial opening, and cross-sections through the midbrain and upper pons disclosed multiple small midline hemorrhages such as are often seen under those circumstances. The whole brain was soft and, on section, contained numerous scattered punctate areas that looked like tiny hemorrhages in the cortex and central white matter. Small blood vessels were greatly congested, but there was no definite exudate in the subarachnoid space. Although the corpus callosum was swollen, as was the rest of the brain, there was no evidence of tumor in it anywhere.

Microscopical examination has shown us an astonishing degree of vascular disease of small arteries of arteriolar size. By contrast, the small cerebral arteries of perhaps 0.3 to 0.5 mm. in diameter were normal, and the capillaries and veins were not remarkable.

The first illustration (Fig. 2) gives an example of the density and distribution of the vascular lesions. They were most numerous in the cerebral cortex and adjacent meninges; the left hemisphere was somewhat more severely involved than the right, but the process was diffuse and bilateral. The arterioles of the white

Figure 2. *Low-Power View (Cresyl Violet Stain), Showing Multiple Arteriolar Lesions in the Cerebral Cortex (Arrows Point to Some of Them).*
Note a normal small artery in the meninges.

matter and central nuclear masses of the brain were much less frequently diseased than those in the cerebral cortex, and those in the cerebellum and brain stem were relatively spared, although typical vascular lesions were seen in these areas as well.

Microscopically, there were severe destructive and inflammatory changes involving the entire thickness of the vessel walls. In some, the wall was transformed into an amorphous, brightly eosinophilic mass, surrounding which, in the adventitia, there were dense accumulations of lymphocytes, histiocytes and multinucleated giant cells (Fig. 3). The necrotic material in the walls stained like fibrin, so that there was "fibrinoid necrosis." Very often, the vessel walls were the site of extensive granuloma formation in which multinucleated giant cells of foreign-body type were numerous (Fig. 4). There were few, if any, eosinophils.

In association with these vascular lesions, there was extensive destruction of nerve cells throughout the cerebral cortex, with increase in the size and number of astrocytes and proliferation of the microglia. Some of the diseased vessels were surrounded by small perivascular intracerebral hemorrhages of varying ages —

FIGURE 3. *High-Power View of an Arteriole (Hematoxylin and Eosin Stain), Showing "Fibrinoid" Necrosis of the Wall, and Inflammatory Infiltration of the Adventitia, with Marked Astrocytic Proliferation in the Surrounding Brain.*

some obviously recent, and others showing accumulations of macrophages laden with hemosiderin.

Dr. Victor is to be congratulated on having arrived at the precise diagnosis that we reached on pathological grounds — namely, a necrotizing and granulomatous arteritis involving small vessels of arteriolar size. We have had very little experience with this condition in this department. There was 1 case, examined by Dr. Charles S. Kubik, about twenty years ago, of a fifty-four-year-old woman who had a rapidly evolving generalized brain disease, likewise thought to be tumor, with death about three weeks after the onset of symptoms. In that case, unfortunately, the autopsy was restricted to examination of the brain. There was a granulomatous arteritis very similar to this, but not as severe.

DR. TAFT: When we heard what was in the brain we reviewed the other organs to see whether we could find some evidence of generalized vasculitis because it seemed logical that this should be a generalized

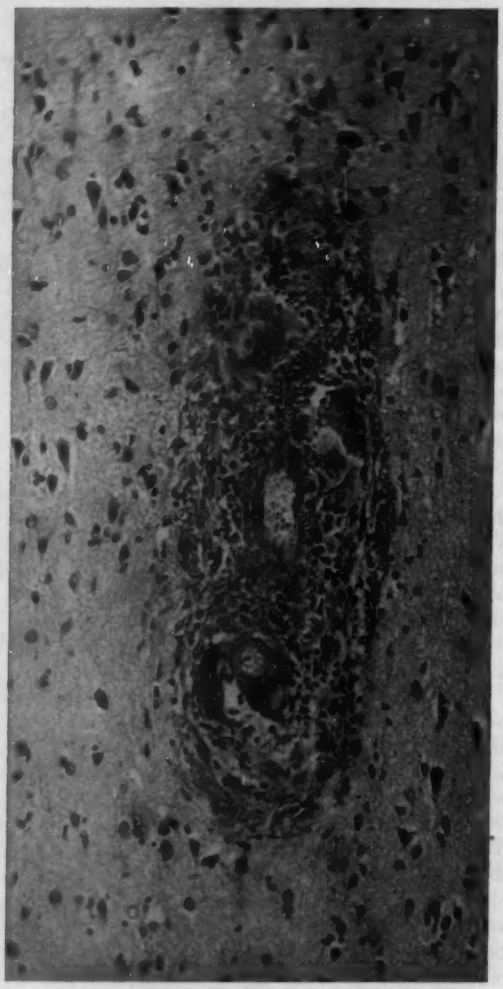

FIGURE 4. *High-Power View of an Arteriole (Hematoxylin and Eosin Stain), Showing Marked Granuloma Formation in the Wall and Numerous Multinucleated Giant Cells. There is astrocytic and microglial proliferation in the surrounding brain.*

disease. The only lesion we have found so far was one in the kidney — an arteriole with a mild inflammatory response around it with two giant cells similar to those Dr. Richardson showed in the brain. Occasionally, other arterioles had a small amount of inflammatory cellular exudate with histiocytes and lym-

phocytes around them, but these were not too different from the ordinary small areas of inflammation in the kidney in arteriolosclerosis.

DR. RAYMOND D. ADAMS: I have only two questions. It has been suggested that this type of small-vessel disease with giant cells is a manifestation of Boeck's sarcoid. Do you believe that that is a tenable diagnosis in this case? Or is it, as several pathologists have maintained, a subvariety of polyarteritis nodosa?

DR. TAFT: Dr. Castleman believes that this is more probably a variety of polyarteritis nodosa; he did not actually mention Boeck's sarcoid when we were discussing the case. It does not look like Boeck's sarcoid to me. The lesions are much more acute, with much more necrosis than one is accustomed to see in sarcoidosis.

DR. ADAMS: I also want to congratulate Dr. Victor on a very astute analysis of the clinical data. I do not know that this diagnosis has ever been made before from clinical data alone. We have struggled with 2 or 3 cases of it on the ward and have never even come close.

ADDENDUM

DR. TAFT: Subsequently, further study of additional sections of lung, kidney, spleen, liver and heart gave no evidence of other vascular lesions or of lesions suggesting the granulomas of sarcoidosis.

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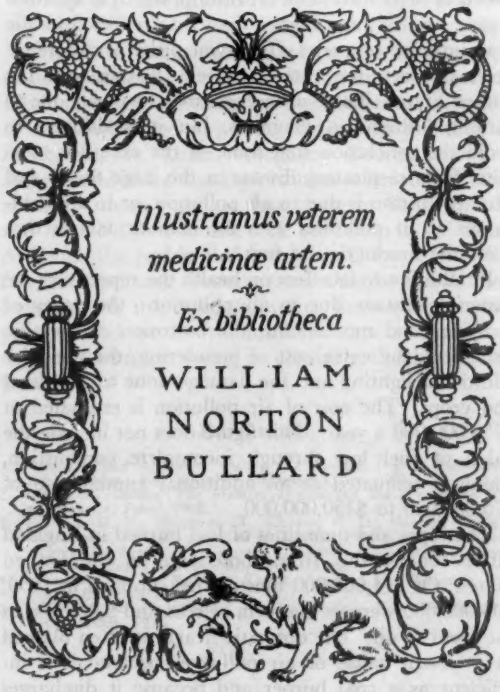

BOOKPLATE COLLECTION OF THE BOSTON MEDICAL LIBRARY

4. Bookplate of William Norton Bullard, M.D. (1853-1931), eminent neurologist, book collector and benefactor and a past vice-president of the Library, who purchased many rare and valuable books on his trips abroad, acquiring a fine neurologic collection as well as medical books of the fifteenth and sixteenth centuries. Some years before his death he made a deed of gift of his books, including such items as the first edition of Holbein's *Dance of Death*, to the Boston Medical Library, where he deposited his incunabula for safe keeping. He also left to the Library $50,000 to be used to build up the collection.

During his life he would not purchase any manuscripts, but when he made his will he changed his mind, leaving $50,000 of which both principal and interest could be used for the purchase of manuscripts and printed books before 1700, making funds available in distressed times and hastened the growth of the collection, now numbering 831 items, without duplication.

The lionlike figure on the bookplate represents the English sheep dog, a breed in which Dr. Bullard was greatly interested.

The New England Journal of Medicine

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY

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BEAVER REPORT ON AIR POLLUTION

THE London "smog" disaster of December, 1952, was responsible for about 4000 deaths.[1] This was not the first occasion on which a prolonged smoke fog had caused a sudden increase in the morbidity and mortality rates of respiratory disease. Previous episodes that have been fully reported include those occurring in the Meuse valley in 1930,[2] when 60 people lost their lives, and in Donora, Pennsylvania in 1948,[3] when there were 20 deaths. The magnitude of the London mortality far exceeded any previous occurrence and aroused considerable public concern. A direct result was the creation of a governmental committee under the chairmanship of Sir Hugh Beaver to enquire into the whole question of air pollution and to make recommendations. The committee, which issued an interim report in December, 1953,[4] has now made its final report.[5]

In discussing the effects of air pollution on health the final report gives tables showing a steady increase in mortality rates from bronchitis and pneumonia when rural areas are compared with towns and cities. It is also noted that a similar relation exists between lung-cancer death rates and urbanization. The report calls attention to the remarkably high death rate ascribed to bronchitis in Great Britain, which is approximately twenty times higher than that reported in the Scandinavian countries. The same order of difference exists between the rates in Great Britain and the United States. These differences may be partly due to varying fashions in diagnosis, but it is difficult to avoid the conclusion that some of the excessive mortality from respiratory disease in the large towns and cities of Britain is due to air pollution, or to a combination of air pollution with the climatic factors that favor the production of fogs.

In addition to its effect on health the report lists the material wastage due to air pollution: the decay of buildings and monuments, the corrosion of metallic structures, the extra cost of laundering, the need for additional lighting and the damage done to farmland and crops. The cost of air pollution is estimated at $750,000,000 a year. This figure does not include the value of fuel lost through incomplete combustion, which is estimated at an additional annual sum of $75,000,000 to $150,000,000.

The types and quantities of fuel burned in England differ considerably from those used in the United States. Of 214,000,000 tons of fuel supplied in 1953, 205,000,000 were in the form of coal and 9,000,000 in the form of oil. The domestic hearth is often blamed as a potent cause of air pollution because it is inefficient as a coal burner and because it discharges smoke at a low level. However, only 18 per cent of Britain's coal was burned in private homes; 31 per cent was used by industry, and 44 per cent by power stations producing electric power and by gas works and coke ovens producing fuel gas and coke. The railroads accounted for the remaining 7 per cent. The

concentration of coal combustion in power stations makes it especially necessary to select sites away from cities and in such a way that the prevailing winds will carry the smoke away. Methods for reducing industrial air pollution by better fueling practice and by the extended use of special appliances are discussed in detail.

The recommendations of the Beaver committee include the prohibition of the emission of black smoke from any chimney (with some specified exceptions as in the metallurgical industry), the extension of smokeless zones in the center of cities and the introduction of "smoke control" zones in which the use of bituminous coal for domestic purposes would be restricted (financial assistance to be provided by local authorities and the Exchequer to householders for the conversion of heating appliances in these areas) and the removal of the present purchase tax of 50 per cent on gas and electric heaters. Also recommended are governmental loans and tax exemption to plants installing efficient new smoke-reducing equipment, the gradual change from coal-burning to coke-burning or other smokeless heaters in domestic dwellings and the strengthening of the laws governing air pollution and their more vigorous enforcement. The need for further research on the health, engineering and chemical aspects is emphasized.

There are useful appendixes on the measurement of air pollution, on chimney design and on measures taken in other countries for the abatement of pollution. The last includes brief sections on pollution in Pittsburgh, St. Louis, Allegheny County and Los Angeles and notes that the ordinances in some of these areas are more rigorous than those of Great Britain and have led to a considerable reduction in pollution. Although the problem of "smog" in Great Britain differs in important respects from that in the United States much information in the Beaver report will prove useful to health administrators and sanitary engineers who are trying to eliminate this health risk here.

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INFLUENZA B

Infection with influenza B can no more be distinguished by clinical signs alone from that due to other strains of influenza virus than specific infections with any of the 3 poliomyelitis viruses can be identified by the unaided senses of the examiner. However, certain clinical and epidemiologic features make influenzal diseases suspect. The pharynx is diffusely injected, and there is commonly a mild erythema of the skin; the patient has a flushed appearance as though he had just returned from the beaches in Florida. The prostration is out of all proportion to physical signs and this makes for a disproportionately high ratio of bed to ambulatory cases in comparison with more localized and commonplace infections of the nasopharynx. It is this feature that makes for a high prevalence of absenteeism in schools and industry. The engulfment of the school, town, city or state is so rapid as to create epidemic conditions within a matter of weeks because of the short incubation period and high infectivity. As every practitioner knows, the diagnosis, which is fraught with difficulty apart from the epidemic context, is made with ease and confidence during an outbreak — during such outbreaks, for example, as closed schools widely in New England during February, 1955. In the words of the American Public Health Association's handbook, *Control of Communicable Diseases in Man*,[1] "Recognition is ordinarily on the basis of symptoms and the presence of an epidemic."

However, to diagnose influenza is not to establish the etiologic agent; that can only be done in the laboratory with paired serums, or more rarely by recovery of the virus itself from nasopharyngeal washings. The ultimate objective of such academic activity as placing a label on the prevalent strain is, of course, to help complete understanding of the natural history of influenza and to identify and harvest the major strains of viruses and prepare an effective vaccine from them.

In a recent analysis of virus isolations of B strains that they recovered in the vicinity of Boston in the past decade Finland and Barnes[2] found evidence of a continuous variation in the antigenic patterns of strains prevalent in 1945 and in 1952; serums drawn from patients convalescing from this form of influenza failed to discriminate in a highly specific manner between the standard Lee and Bon strains of influenza B on the one hand and the more recently isolated strains of that type on the other and did not distinguish the A from the B strains.

The application of these results to immunization cannot be evaluated with confidence. However, from the fact that the serums of adult patients convalescent from infection with influenza B virus in recent epidemics yielded similarly high titers of antibody against the Lee, the Bon and the epidemic strains suggests that eventually a polyvalent vaccine for adults might be prepared with the antigen representing its influenza B component derived from recent strains of influenza A or B viruses.

The more specific antibody responses of children against the epidemic strains was interpreted to indicate that the most recent strain should provide vaccine as efficient as — or perhaps better than — the older, so-called "standard strains." The difficulty, of course,

would be to prepare such a vaccine in time to do the country's youth any good.

If the whole natural history of influenza is a kaleidoscopic succession of mutations it is indeed doubtful if any vaccine will ever be satisfactory. The facts at present justify neither extreme optimism nor pessimism but warrant further investigations of the type first undertaken by Smith, Andrewes and Laidlaw in England, by Burnet and his colleagues in Australia and by Francis, Magill and others in the United States.

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FREE PRIVATE LIBRARY

Before the subject of reprints (re requests for), discussed in the issue of December 16, is considered to be exhausted, statistical information newly received deserves some comment. The recipient of a number of requests, who supplied the data, suggested as possible titles for the further elaboration of this topic "The Reprint Racket" or "What Price Courtesy?"

The figures comprise a breakdown of 614 requests for reprints of an article originally published in the *Journal*. Twenty-six per cent only, or 161 of the requests, were personal communications, either by postcard or by letter. The remaining 453, or 74 per cent, consisted of form letters or postcards untouched by the ink of human kindness except where the title of the reprint was written in or typed. Unclassified is a request, written by hand, but including neither name nor address.

For a more detailed analysis the following statistical evidence is submitted. Of 175 physicians giving a hospital address only, 38 requested a reprint by personal communication, whereas 137 considered that a form postcard implied sufficient courtesy, or constituted in itself a flattering recognition of the value of the author's work. Practicing physicians, or at least those giving an office address only, more used, perhaps, to the amenities of human intercourse, preferred the personal communication; of 127, 72 addressed their requests by letter, and only 55 by form postcard. But alas for the abiding places of academic culture! Of 173 physicians giving medical-school or hospital and medical-school addresses only, 154 were content to collect their libraries through the medium of the printed card, as opposed to only 19 who preferred the more genial personal communication.

Interestingly enough, only 13 medical libraries were among those requesting reprints. These, combined with 24 pharmaceutical firms, 33 Veterans Administration hospitals, 31 laboratories, boards of health, foundations and Army and Navy hospitals, and 37 foreign sources comprised a group of 138 requests, of which 32 were by personal letter or card.

Multiple requests assumed some significance in the total. Thus, among the individuals, 16 doctors requested 2 reprints, 3 requested 3 each, and 1 physician would have been completely satisfied with no less than 4. Institutions or their personnel were the most demanding, however. Five requests came from each of 4 hospitals, and 6 from each of 2 hospitals; 8 came from 1 800-bed institution, 9 from one of 600 beds, and 13 from one of 185 beds. Nor were the medical schools far behind, with an average of 3.2 requests from the 54 schools represented. Five requests came from 2 of these, 6 from 3, and 7, 10 and 13 from 1 each.

Probably these figures would have been completely different had reprint solicitors in general realized that they were, in a sense, requesting the equivalent of cash donations, postage prepaid, for their private libraries, from authors who must often be total strangers. Such solicitations might at least be put in a form that would acknowledge the fact of a favor being asked.

G. G. BUSHMAN, 1933 - 1955

Considerable anxiety is being expressed, according to a news release from the American Medical Association, over the death of Bushman, the aging gorilla (*Gorilla gorilla*) of Chicago's Lincoln Park Zoo. Bushman at twenty-two was definitely on life's more distant slope, although not yet senile; a sort of elder statesman among gorillas. Autopsy showed a little cerebral sclerosis and a bit of renal trouble, — nothing much, — a bad tooth or two, a trace of gingivitis and some anthracosis. The cause of death was congestive failure with a heart resembling that of beriberi.

Bushman, 6 feet 2 inches in his stocking feet, had gone from a bouncing 38 pounds in 1930 to a paunchy 550 a year ago; despite strict attention to diet he still weighed in at a quarter ton before death. What concerns humanity is the fact that Bushman, like other pithecanthropi pent, had been unable to procreate, a failing attributed to some unknown nutritional defect. With gorillas slowly dying out on their native African heath, their extinction in the zoologic gardens of the world will render them extinct in very fact — a tragic circumstance only partly relieved by the knowledge that the ubiquitous *Gorilla humana* shows no signs of extinction at all.

Tartar emetic, given secretly, in doses of from five to ten grains, is recommended by Dr. Gilbert, in the London Lancet, as a remedy for drunkenness. — Apiol, the immediate or active principle of parsley, is suggested as a substitute for quinine.
Boston M. & S. J., *April 19, 1855*

MASSACHUSETTS MEDICAL SOCIETY

TREASURER'S REPORT COVERING DISTRICT DISTRIBUTION

The Committee on Finance has voted to distribute the sum of $6,000 for the year 1955 to the district societies toward defraying their operating expenses. The total number of payments received by March 1, in time to count for the distribution, was 4718 — an increase of 213 over 1954. The amount for each paid member comes to $1.2717.

The following table gives the number of payments as of March 1 for each district. The actual amount of the distribution to each district is shown as of March 22, 1955.

District	No. Reported Paid	Amount Distributed
Barnstable	57	$ 72.49
Berkshire	131	166.60
Bristol North	69	87.76
Bristol South	188	239.08
Charles River	443	563.37
Essex North	173	220.01
Essex South	258	328.10
Franklin	43	54.69
Hampden	339	431.11
Hampshire	56	71.23
Middlesex East	141	179.31
Middlesex North	110	139.90
Middlesex South	552	701.98
Middlesex West	120	152.61
Norfolk	722	918.17
Norfolk South	165	209.84
Plymouth	132	167.87
Suffolk	589	749.04
Worcester	339	431.11
Worcester North	91	115.73
	4,718	$ 6,000.00

ELIOT HUBBARD, JR., M.D., *Treasurer*

CIRCULAR OF ADVANCE INFORMATION

Copies of the *Circular of Advance Information for Councilors* for the May 16 meeting of the Council are available, as long as the supply lasts, to all fellows who apply to the Secretary, 22 Fenway, Boston.

DEATH

REED — Laurence B. Reed, M.D., of Plymouth, died on March 24. He was in his seventy-fifth year.

Dr. Reed received his degree from Harvard Medical School in 1907. He was a fellow of the American Medical Association.

He is survived by a daughter, a son and a brother.

CORRESPONDENCE

OSMOTIC PRESSURE IN DIABETES INSIPIDUS

To the Editor: We should like to comment on the letter of Dr. Charles H. Burnett in the February 17 issue of the *Journal* regarding our paper entitled "Determination of Osmotic Pressure in Diabetes Insipidus: A new diagnostic test."

Dr. Burnett states that the proposed test is cumbersome and complicated and that patients with psychogenic polydipsia and polyuria are apt to give false-positive reactions. He furthermore maintains that determination of the urinary specific gravity will give information comparable to simultaneous measurement of the osmotic pressure of the blood and urine.

Actually, the procedure is done within a few minutes by laboratory technicians using either a Beckman type of thermometer (cyroscope) or the Fiske apparatus. We have made these determinations on many water-loaded patients and in no case was a ratio of solute concentration in the urine to that in the blood less than one obtained under the stated conditions. This was not included in our data since it had previously been recorded in the literature by Baldes and Smirk (*J. Physiol.* **82**:62-74, 1934), and our controls would have been superfluous.

Undoubtedly, the nonspecificity of using merely the specific gravity of the urine as a test for diabetes insipidus is well known, and low specific gravity should be viewed only as presumptive evidence for posterior pituitary insufficiency. In our experience values as high as 1.016 have been recorded after prolonged fasting, leaving the clinicians with an uncomfortable patient and confusing data. The fact that the pH, temperature and protein content and the various solutes (sodium, potassium, calcium, creatinine, urea and so forth) contribute so differently to the specific gravity should unmistakably indicate that specific gravity is, at best, only a rough index of urinary concentration.

The borderline cases and those in which both anterior and posterior pituitary insufficiency are present may go unrecognized unless the total blood solutes as well as urinary solutes are measured simultaneously.

LEONARD S. DREIFUS, M.D.
MARTIN N. FRANK, M.D.
SAMUEL BELLET, M.D.

Philadelphia

REGARDING DYSLEXIA

To the Editor: The article entitled "Pathogenesis of Reading Disability" in the February 10 issue of the *Journal* has been read with a great deal of interest. From the point of view of a lay reading instructor the paper is excellent. I am afraid, however, that it will make the average physician say, "Interesting, but what does it have to do with me?" This would be most unfortunate because it is believed that in many cases of reading disability the cause may be found by an intelligent physician willing to spend a little time with the patient.

The obvious causes of dyslexia, diagnosable at physical examination, are poor hearing, poor vision, diplopia and neurologic lesions, such as postencephalitic paralysis agitans, and may make reading difficult because of inability to control the head movement.

Even the more esoteric forms of reading difficulty that come to the reading therapist can be diagnosed by the family practitioner if he takes care with the history and physical examination. There are several good medical articles on how to proceed with the necessary examination, such as that by Robert M. West in *Brennemann's Practice of Pediatrics* (Vol. 4, Chapter 14, Page 32).

It is thought that viewing all children who are unable to read as potential psychiatric patients is like the five blind men "viewing" an elephant. The one with his hands on the tail said, "It is a whip." The one with his hand on the leg said, "It is a column." The one with his hands on the trunk said, "It is a hose." And so forth. Dyslexia is a many-faceted problem that can best be solved by the family doctor. After the cause of the difficulty is known, the child, if necessary, may be referred to the reading clinic for appropriate treatment.

ROY SWARTOUT, III, M.D.

El Monte, California

REVOCATION OF LICENSE

To the Editor: At the meeting of the Board of Registration in Medicine held January 27, 1955, it was voted to revoke the registration of Dr. Roland O. Parris, of Tucson, Arizona.

ROBERT C. COCHRANE, M.D.
Secretary

State House
Boston

BOOK REVIEW

It's Not All in Your Mind. By H. J. Berglund, M.D., and H. L. Nichols, Jr. 8°, cloth, 343 pp. Greenwich, Connecticut: North Castle Books, 1953. $3.95.

This delightful book is not too seriously presented, but there is an undertone of serious meaning that the careful reader will not escape. It illustrates *de facto* a current quip now going the rounds in psychiatric circles to the effect that a physician is compelled to tell a patient, "I am sorry, but it's all in your body!" Written for the large section of the public that is interested in health, this book is quite basic in its application; beginning with body, brain and nervous system, it includes sections on reflexes and suggestion, but then it broadens out and in a general manner deals blandly with the topics of allergy, foods and drugs, furniture, internal chemistry and other matters that are of equal concern to patient and physician. It represents a growing tendency to spread medical knowledge more generously to a multitude of suffering persons, all of whom are eager for knowledge and improvement.

MERRILL MOORE, M.D.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Physiology and Biochemistry of the Skin. By Stephan Rothman, M.D., professor of dermatology, University of Chicago. 8°, cloth, 741 pp., with illustrations. Chicago: University of Chicago Press, 1954. $19.50.

The author, with the assistance of six collaborators, has made a comprehensive survey of the existing knowledge on the physiology and biochemistry of the skin. Extensive bibliographies are appended to the chapters (in 1 case numbering 501 references), and there are indexes of names and subjects. The publishing is excellent. The book is recommended for all medical libraries as an important reference source and to all dermatologists.

Endemic Goiter: The adaptation of man to iodine deficiency. By John B. Stanbury, M.D., Hector Perinetti, M.D., Juan Itoiz, Ph.D., and Enrique B. Del Castillo, M.D. 8°, cloth, 209 pp., with illustrations. Cambridge, Massachusetts: Harvard University Press, 1954. $4.00. (No. 12, *Harvard University Monographs in Medicine and Public Health.*)

This report summarizes the studies carried out on goitrous patients in an area in western Argentina known to be deficient in iodine. The text is in three parts. The first describes the Mendoza epidemic. The second deals with functional interrelations, and the third with the dynamics of iodine metabolism. Lists of references are appended to the chapters and there is a good index. The book should be in all collections on goiter.

Lipoproteine ed eparina nel quadro umorale della chimiopatogenesi dell' aterosclerosi. By F. M. Antonino; G. Piva; L. Salvini; and A. Sordi. 8°, paper, 96 pp., with illustrations. Florence: Casa Editrice Macri, 1953. (Supplement No. 1 to *Giornale di Gerontologia.*)

The authors present the results obtained from the use of an improved method of paper electrophoresis for the study of the metabolism of plasma proteins in experimental and human atherosclerosis. The effect of heparin on normal and atherosclerotic subjects is studied in detail, and the conclusion is reached that heparin treatment is practical. The literature is surveyed, and there is a bibliography of 138 titles. There are also English and French summaries of the Italian text.

Fundamentals of Neuropathology. By William Brooks Dublin, M.D., chief, Laboratory Service, Veterans Administration Hospital, associate professor of pathology, University of Colorado School of Medicine, and consultant in neuropathology, Denver General Hospital, Denver, Colorado. 4°, cloth, 685 pp., with illustrations. Springfield, Illinois: Charles C Thomas, 1954. $18.50.

The author's aim is to present neuropathology as a component of general pathology as practiced in hospitals not specializing in neurology or psychiatry. He has done so adequately, using standard methods of staining and examination. The illustrations are adequate, and all aspects of neuropathology are covered. The book is sponsored by the Veterans Administration but much of the preparation was done at the Indianapolis General Hospital. There are chapters on autopsy technic and tissue staining, and nearly 500 references carry the subject up to 1953. There are a number of typographic and structural errors in the text, and the index is somewhat faulty.

Diagnosis and Localization of Brain Tumors: A clinical and experimental study employing fluorescent and radioactive tracer methods. By George E. Moore, M.D., Ph.D., Markle Scholar in the Medical Sciences, director, Roswell Park Memorial Institute, and asscciate professor of surgery, University of Buffalo School of Medicine. 8°, cloth, 217 pp., with 66 illustrations, 8 tables and 6 plates. Springfield, Illinois: Charles C Thomas, 1953. $10.50.

This highly technical work covers a newly opened field: the use of radioactive isotopes in the delineation of brain tumors. The author is an acknowledged leader in these experimental studies. By "tagging" certain dyes, for which some intracranial tumors have an affinity, he was able to establish a heavy concentration of radioactivity in the lesions, thus adding the painless method of isotope encephalometry to encephalography, ventriculography and arteriography as a diagnostic measure. This is now leading to the use of neutron-capturing isotopes for clinical therapy, just beginning to be visualized as the volume went to press. The book is well illustrated and carefully written and carries a full bibliography. It is a landmark in a rapidly expanding field.

Die Narkose: Ein Lehr—und Handbuch. Edited by Prof. H. Killian and Prof. Dr. H. Weese, with the collaboration of Dr. W. Irmer and Dr. F. H. Koss and with contributions by Prof. Dr. F. Hahn, Doz. Dr. W. Rummel and Dr. R. Vormann. 4°, Bd., 1003 pp., with 412 illustrations. Stuttgart: Georg Thieme, 1954. DM 170. (Distributed by Intercontinental Medical Book Corporation, New York City.)

This is a comprehensive treatise on anesthesia, covering all aspects of the subject. The literature has been surveyed, and lists of references — some extensive — are appended to the various topics. There is a good index. The book is recommended for all collections on the subject.

Gehirn und Auge: Grundriss der Ophthalmo-Neurologie. By Dr. Dr. h.c. Robert Bing, professor in ordinary of neurology, Universität Basel, and Dr. Roland Brückner, lecturer in ophthalmology, Universität Basel. Fifth edition revised. 8°, Bd., 248 pp., with 147 illustrations. Basel: Benno Schwabe and Company, 1954. Fr. 28. – – (Distributed by Intercontinental Medical Book Corporation, New York City.)

This new edition of a well known monograph on the neurology of the eye has been completely revised and brought up to date. The illustrations are excellent. There is a good index. The book should be in collections on the subject.

Altern und Krankheit: Grundlagen einer bioheutischen Nosologie. By Professor Dr. Med. Max Bürger, director, Medizinische Universitätsklinik in Leipzig. Second edition. 8°, Bd., 600 pp., with 285 illustrations and tables. Leipzig: Georg Thieme, 1954. DM 40.

Dr. Bürger has written an extensive book on the diseases of the aged. The first part of the text, comprising 279 pages, is devoted to the general and special physiology of the aged, and the second to the diseases of the organs and systems of the body. The literature has been surveyed, and there are indexes of names and subjects. The book should be in all collections on the subject.

Antibiotika-Fibel. Indikation und Anwendung der Chemotherapeutika und Antibiotika. By Dr. A. M. Walter, in charge of the ward for infectious diseases and of the bacteriologic laboratory, Medizinische Universitätsklinik Freiburg i. Br.; and Prof. Dr. Ludwig Heilmeyer, director, Medizinische Universitätsklinik Freiburg i. Br. 8°, Bd., 813 pp., with tables. Stuttgart: Georg Thieme, 1954. DM 79. (Distributed by Intercontinental Medical Book Corporation, New York City.)

The author has written a comprehensive summary of the indications and use of the antibiotics and chemotherapeutic agents in the treatment of disease. The text is divided into two parts: general and clinical. Two thirds of the text is devoted to an extensive coverage of the diseases of various systems and organs of the body. The pertinent literature through 1953 is surveyed, and long bibliographies are appended to the various sections and diseases. (Infectious diseases has 21 pages, and tuberculosis 142 references.) There is a good index. The book is recommended for all medical libraries as a reference source.

Laboratory Aids in Endocrine Diagnosis. By Roberto F. Escamilla, M.D., associate clinical professor of medicine, University of California School of Medicine. 8°, cloth, 131 pp., with 21 illustrations. Springfield, Illinois: Charles C Thomas, 1954. $4.75. (No. 212, *American Lecture Series.*)

The author has listed the tests that have proved to be of clinical value and emphasizes the fact that they should be used only as aids to a thorough clinical study. In a final chapter the data listing the various endocrine diseases and the appropriate laboratory findings are recapitulated. Lists of references are appended to the chapters, and the text is well illustrated.

The Laboratory Diagnosis of Leptospirosis. By J. W. Wolff, M.D., professor of tropical hygiene, University of Wageningen, and bacteriologist, Institute of Tropical Hygiene and Geographical Pathology, Royal Tropical Institute, Amsterdam, The Netherlands. 8°, cloth, 99 pp., with 5 illustrations and 7 tables. Springfield, Illinois: Charles C Thomas, 1954. $3.75. (No. 183, *American Lecture Series.*)

Leptospiral infections have been found in all countries of the world, and in addition to Weil's disease a number of infections caused by pathogenic leptospirae have been detected. They were found to be morphologically and culturally indistinguishable from the Weil leptospira, but serologically different. It was also observed that rodents, dogs, pigs and cattle could become renal carriers and could form a source for human infection.

The literature is surveyed, and there is a bibliography of 10 pages and an index.

Depression. Edited by Paul H. Hoch, M.D., New York State Psychiatric Institute, Columbia University College of Physicians and Surgeons; and Joseph Zubin, Ph.D., New York State Psychiatric Institute, Department of Psychology, Columbia University. 8°, cloth, 277 pp., with illustrations. New York: Grune and Stratton, 1954. $5.50. (The proceedings of the forty-second annual meeting of the American Psychopathological Association, held in New York City, June, 1952.)

At this meeting 15 papers were presented on various aspects of depressive disorders, including manic-depressive psychosis and the various methods of treatment used for the disorders. Also included is the president's address, "Biometric Methods in Psychopathology." There is a list of members of the Association and a good index.

Manual of Urology. By Alec W. Badenoch, M.A., M.D., Ch.M. (Aberd.), F.R.C.S., surgeon to St. Peter's Hospital for Stone and Other Genitourinary Diseases, assistant surgeon to the Royal Hospital of St. Bartholomew, visiting urologist to the Royal Masonic Hospital and to the Samaritan Hospital for Women, consulting urologist to the King Edward VII's Hospital for Officers (Sister Agnes Founder) and to the Association of Retired Naval Officers, Hunterian Professor, Royal College of Surgeons, 1948, lecturer in surgery at the Medical College of the Royal Hospital of St. Bartholomew, and lecturer in urology at the Institute of Urology, University of London. 8°, cloth, 555 pp., with 343 illustrations. New York: Grune and Stratton, 1954. $15.75.

The author has written a practical manual on urology for general surgeons containing the essentials of symptomatology, pathology, diagnosis and treatment based on his own practice and that of the St. Peter's Hospital for Stone and Other Genitourinary Diseases. Short lists of references are appended to the chapters, and there is a good index. The illustrations, including some full-page color plates, are excellent. The printing was done in Great Britain.

The Scourge of the Swastika. A Short History of Nazi War Crimes. By Lord Russell of Liverpool, C.B.E., M.C. 8°, cloth, 259 pp., with 16 pp. of halftone illustrations. New York: Philosophical Library, 1954. $4.50.

NONCLINICAL NOTES

CANCER AWARDS

The annual award of the Massachusetts Division of the American Cancer Society has been granted posthumously to the late Dr. Ira T. Nathanson, formerly associate clinical professor of surgery, Harvard Medical School, and associate visiting surgeon, Massachusetts General Hospital.

CARNEY HOSPITAL

Dr. John J. Todd, instructor in surgery at Tufts College Medical School, from which he graduated in 1927, has been appointed chief of surgery at the Carney Hospital.

ACADEMY GOLD MEDAL

Dr. Edward T. Whitney, of Boston, has received the 1955 honor award and gold medal of the International Academy of Proctology.

NOTICES

AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY

The annual meeting of the American Electroencephalographic Society will be held at the Palmer House, Chicago, June 10-12.

There will be symposiums on microelectrodes, with Dr. Herbert H. Jasper as chairman, and on clinical electroencephalographic interpretation (head injuries), with Dr. Frederic A. Gibbs as chairman.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

Oral and clinical examinations (Part II) of the American Board of Obstetrics and Gynecology will be held at the Edgewater Beach Hotel, Chicago, May 11 through 20.

Formal notice of the exact time of each candidate's examination will be sent him in advance. Candidates who participated in Part I examinations will be notified of their eligibility for Part II examinations as soon as possible.

WOMAN'S AUXILIARY TO THE AMERICAN MEDICAL ASSOCIATION

All members of the Woman's Auxiliary to the American Medical Association, their guests and guests of physicians attending the convention of the American Medical Association, Atlantic City, New Jersey, June 6-10, are invited to participate in all social functions and attend the general meetings of the Auxiliary. Headquarters will be at Haddon Hall Hotel. Tickets for the activities will be available at the registration desk only. Early registration is requested.

AMERICAN PROCTOLOGIC SOCIETY

The annual meeting of the American Proctologic Society will be held at the Hotel Statler, New York City, June 1-4.

Among the speakers will be Drs. Henry T. Randall, Benjamin G. Shafiroff, E. A. Rovenstein and Frank L. Meleny. All sessions are open to the medical profession.

CIVIL SERVICE COMMISSION EXAMINATION FOR TECHNICAL EDITORS AND WRITERS

The United States Civil Service Commission announces that positions for technical editors and writers in the fields of physical sciences and engineering and medical sciences are open in the Potomac River Naval Command and other federal agencies in Washington, D. C. No written examination is required, but applicants must have had appropriate experience or a combination of education and experience. Salaries range from $3,410 to $10,800 a year. Application forms and further information may be obtained from many post offices and the United States Civil Service Commission, Washington 25, D. C.

SOCIETY MEETINGS AND CONFERENCES

April. Postgraduate Medical Institute. Page 451, issue of September 9.

April–May. Sanitary Engineering Center Training Programs. Page 122, issue of July 15.

April 14–28. Consultation Clinics for Crippled Children in Massachusetts. Page 551, issue of March 31.

April 14–May 26. Boston City Hospital. House Officers' Lectures. Page 509, issue of March 24.

April 18. Hartford Medical Society. Page 289, issue of February 17.

April 20–May 25. Lahey Clinic Lectures. Page 461, issue of March 17.

April 20–June 15. Boston State Hospital. Psychiatry Seminars. Page 461, issue of March 17.

April 21 and 22. New York Academy of Medicine (Eastern States Health-Education Conference). Page 922, issue of November 25.

April 22. Boston University Surgical Seminar. Page 603, issue of April 7.

April 23. American Congress of Physical Medicine and Rehabilitation. Page 603, issue of April 7.

April 23. Massachusetts State Society of Medical Technologists. Page 461, issue of March 17.

April 23–29. Industrial Health Conference. Page 509, issue of March 24.

April 25. Yale Medical Society. Page 603, issue of April 7.

April 25–30. American College of Allergists. Page 462, issue of March 17.

April 26. Hampden District Medical Society. Page 603, issue of April 7.

April 26. South End Medical Club. Page 603, issue of April 7.

April 26. Harvard Medical Society. Page 509, issue of March 24.

April 26. Alpha Omega Alpha Lecture. Page 554, issue of March 31.

April 27. Middlesex West District Medical Society. Page 603, issue of April 7.

April 27–30. Instituto Nacional de Cardiología de México. Page 554, issue of March 31.

April 28–30. American Goiter Association. Page 329, issue of February 24.

April 30. State University College of Medicine at New York City. Page 289, issue of February 17.

April 30. Phi Delta Epsilon Fraternity. Graduate Club of Boston. Page 461, issue of March 17.

May 4 and 5. American Psychosomatic Society. Page 286, issue of August 12.

May 6–8. Student American Medical Association. Page 461, issue of March 17.

May 7. Middlesex South District Medical Society. Postgraduate Course. Page 758, issue of October 28.

May 13 and 14. American Association for Cleft Palate Rehabilitation. Page 461, issue of March 17.

May 13–15. American Academy of Dental Medicine. Page 554, issue of March 31.

May 17–19. Massachusetts Medical Society. Annual Meeting. Hotel Statler, Boston.

May 18–20. American College of Cardiology. Page 414, issue of March 10.

May 23–27. American Trudeau Society. Page 462, issue of March 17.

May 29–June 2. American Society of X-Ray Technicians. Page 553, issue of March 31.

June 1–4. American Proctologic Society. Notice above.

June 1–5. American College of Chest Physicians. Page 553, issue of March 31.

June 5 and 6. American Board of Physical Medicine and Rehabilitation. Page 794, issue of November 4.

June 6–10. Woman's Auxiliary to the American Medical Association. Page 647.

June 7–9. United States Public Health Service Medical-Officer Examinations. Page 509, issue of March 24.

June 10–12. American Electroencephalographic Society. Page 647.

June 21–25. National Association for the Prevention of Tuberculosis. Page 540, issue of March 25.

July, August and September. Beth Israel Hospital Course. Page 509, issue of March 24.

July 10–16. Congress of Nobel Prize Winners. Page 510, issue of March 24.

July 11–15. Symposium on Tuberculosis. Page 509, issue of March 24.

August 28–September 2. American Congress of Physical Medicine and Rehabilitation. Page 157, issue of January 27.

October 6–8. Academy of Psychosomatic Medicine. Page 509, issue of March 24.

October 22–26. American Heart Association. Scientific Session. Page 603, issue of April 7.

October 23–27. American Institute of Dental Medicine. Page 414, issue of March 10.

November 6–13. Second International Congress of Allergology. Page 157, issue of January 27.

November 19–21. American Association of Blood Banks. 8th Annual Meeting. Palmer House, Chicago, Illinois.

November 29–December 2. Interim Session of the American Medical Association. Boston.

Calendar for the Week Beginning Thursday, April 21

Thursday, April 21

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:45–9:45 a.m. Cardiac Grand Rounds. Yamins A. Beth Israel Hospital.
*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds, Robert Breck Brigham Hospital.
*10:00–11:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Thoracic Conference. Spontaneous Pneumothorax and Other Thoracic Emergencies. Dr. Harrison Black. Main Amphitheater, Peter Bent Brigham Hospital.
*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*12:00 m.–1:00 p.m. Surgical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*12:00 m.–1:30 p.m. Boston City Hospital Teaching Conference. Inertia and Dystocia. Dr. Daniel McSweeney. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*12:15–1:15 p.m. Orthopedic Clinic. Amphitheater, Peter Bent Brigham Hospital.
*4:00–5:00 p.m. Pediatric Seminar. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*7:00 p.m. Boston City Hospital. House Officers' Association. Cranial Arteritis. Dr. George A. Schumacher. New Cheever Amphitheater, Dowling Building, Boston City Hospital.

Friday, April 22

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
9:30 a.m.–4:30 p.m. Boston University Surgical Seminar. Cheever Amphitheater, Boston City Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–1:00 p.m. Medical Grand Rounds. Dr. Proger and Staff. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*4:00–5:00 p.m. Child Psychiatry. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*4:00–6:00 p.m. X-Ray Conference. Dr. Merrill Sosman. Stearns Auditorium, New England Center Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Morton Street, Jamaica Plain.

Saturday, April 23

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Anesthesia Conference. Dr. Etsten. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:00–10:30 a.m. Surgical Grand Rounds. Dr. Child and Staff. Stearns Auditorium, New England Center Hospital.
*9:30 a.m. American Congress of Physical Medicine and Rehabilitation. Hotel Lenox, Boston.
10:00 a.m.–12:30 p.m. Boston City Hospital Alumni Association. Clinical Meeting. Shortell Conference Room and Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Hematology Clinic. Dr. William Dameshek. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.

(Concluded on page xxvi)

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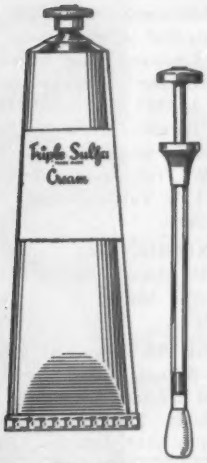

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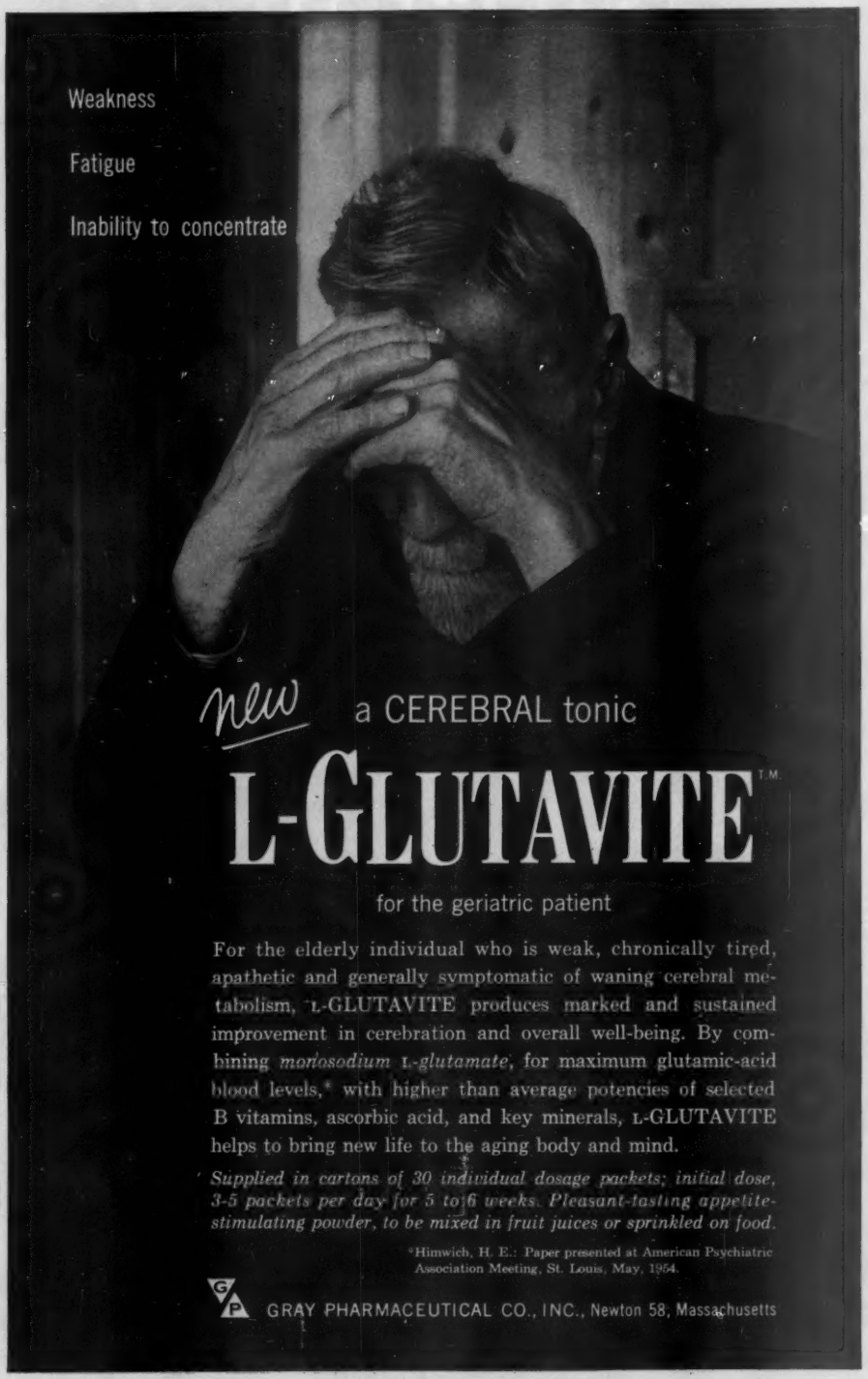

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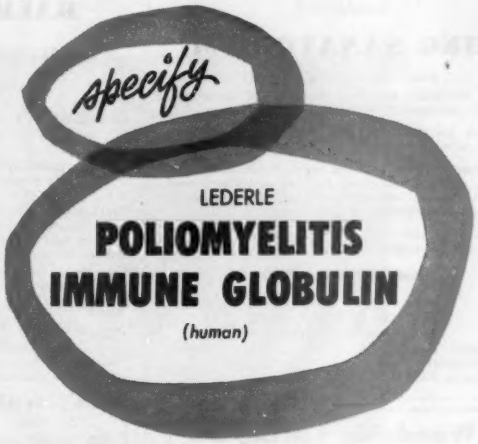

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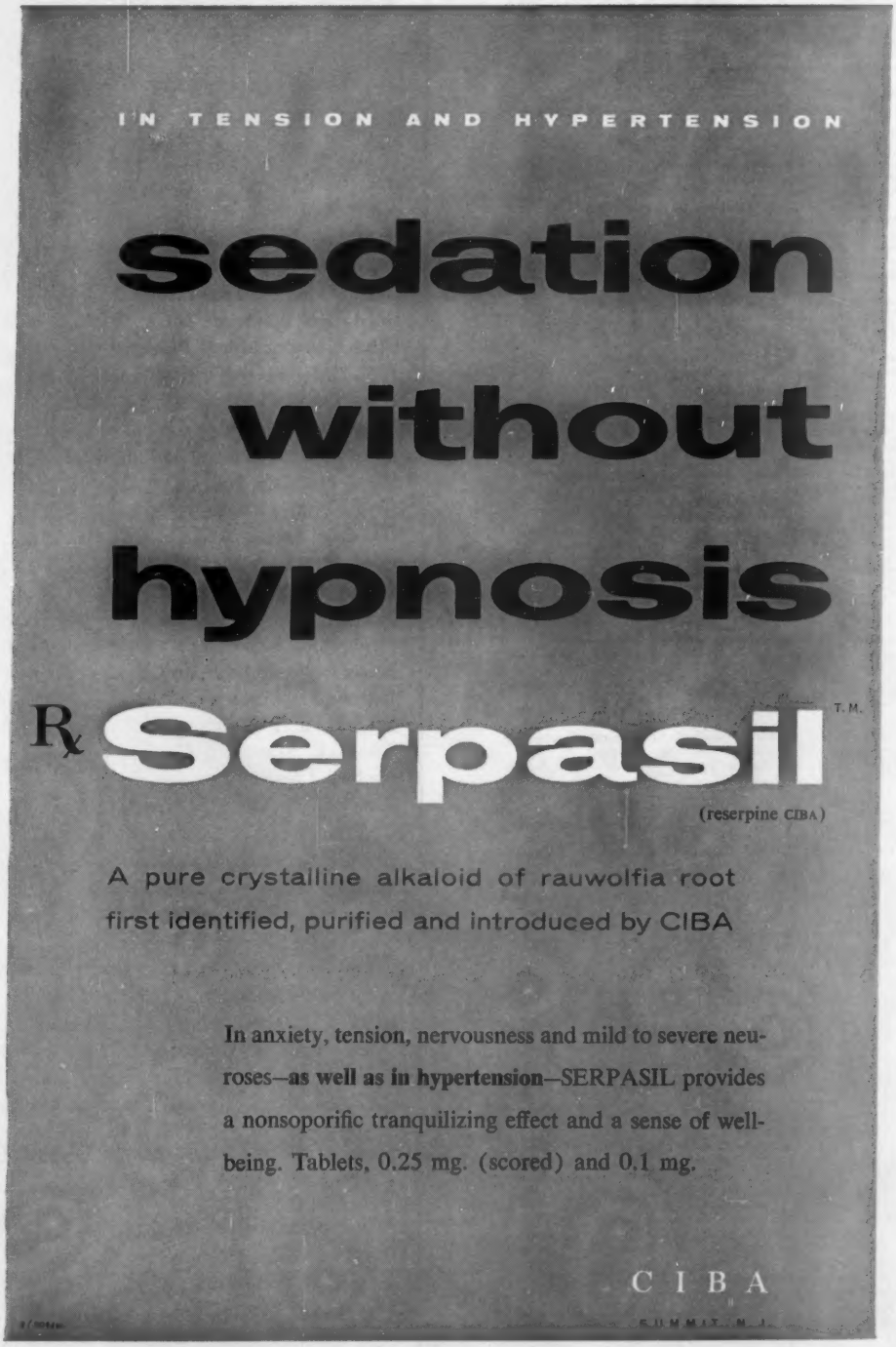
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MONDAY, APRIL 25

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by Entire Surgical Staff and Anesthesia Staff. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m.–1:00 p.m. Medical-Pathological Conference. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*4:00 p.m. Clinicopathological Conference. Pathology Conference Room, Beth Israel Hospital.
*4:00–5:00 p.m. Surgical Pathology. Dr. MacMahon. Stearns Auditorium, New England Center Hospital.
*4:00–5:30 p.m. Anesthesiology Conference. Choice of Anesthesia. Dr. Vandam. Surgical Conference Room, Peter Bent Brigham Hospital.
*5:00–6:30 p.m. Anesthesia Group of the Lahey Clinic. Joslin Auditorium, New England Deaconess Hospital.
5:15 p.m. Staff Meeting. Harris Hall. New England Deaconess Hospital.
*7:00–9:00 p.m. Slide Seminar in Pathology. Dr. MacMahon. Stearns Auditorium, New England Center Hospital.

TUESDAY, APRIL 26

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
12:00 m. South End Medical Club. Veterans Administration Hospital, 150 South Huntington Avenue, Jamaica Plain.
*12:00 m. Pediatric Grand Rounds. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*12:00 m.–1:00 p.m. Endocrine Conference. Dr. Astwood. Stearns Auditorium, New England Center Hospital.
*12:00 m.–1:00 p.m. Pediatric Grand Rounds. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
12:30–1:30 p.m. Medical Journal Club. Joslin Clinic, New England Deaconess Hospital.
*4:00–5:30 p.m. Anesthesia Conference. Dr. Etsten. Stearns Auditorium, New England Center Hospital.
*5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.
*5:00–6:00 p.m. Service Meeting followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.
6:30 p.m. Hampden District Medical Society. Rovelli's, 1396 Boston Road, Springfield, Massachusetts.

WEDNESDAY, APRIL 27

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:00–10:00 a.m. Surgical Grand Rounds. Massachusetts Memorial Hospitals.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Orthopedic Grand Rounds. Bigelow Amphitheater, White 3A, Massachusetts General Hospital.
*11:00 a.m. Boston State Hospital. Psychiatry Seminar. Conscience and Mental Health. Rt. Rev. Thomas J. Riley. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Neurology, Neurosurgery and Psychiatry. Drs. Sullivan, B. Selverstone and Hope. Stearns Auditorium, New England Center Hospital.
*12:00 m.–1:00 p.m. Clinicopathological Conference. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:00 m.–1:00 p.m. Roentgen Diagnostic Conference. 5th-floor teaching unit, Beth Israel Hospital.
*12:15 p.m. Vascular Rounds. Drs. Edward A. Edwards and Chilton Crane. D-Main, Peter Bent Brigham Hospital.
*12:30 p.m. Weekly Pathological Meeting. Joslin Auditorium, New England Deaconess Hospital.
12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*1:00 p.m. Massachusetts General Hospital Hand Clinic. The Clinics of the Massachusetts General Hospital.
*2:00 p.m. Rectal Clinic. Peter Bent Brigham Hospital.
*2:00–5:00 p.m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.
*4:00–6:00 p.m. Overholt Thoracic Conference. Joslin Auditorium, New England Deaconess Hospital.
*6:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
6:30 p.m. Middlesex West District Medical Society. Wayside Inn, Sudbury.
*7:30–9:30 p.m. Lahey Clinic Lecture. Breast Tumors. Drs. Cornelius E. Sedgwick, Ferdinand Salzman and William Meissner. Joslin Auditorium, New England Deaconess Hospital.

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1. Hyman, S., and Rosenblum, S. H.: Illinois M. J. 104:257, 1953.
2. Piper, C. E., and Nicklas, F. W.: Industr. Med. 23:510, 1954

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